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OBSERVATIONS UPON FILARIA PHILIPPINENSIS AND ITS DEVELOPMENT IN THE MOSQUITO.

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INTRODUCTION.

In a special report submitted to the Surgeon-General of the Army in May, 1906, and published in the American Journal of the Medical Sciences in September of that year, we described a new blood filaria of man, to which we gave the name *Filaria philippinensis* sp. nov. because of its occurrence in a native of the Philippine Islands.

We considered that this filaria represented a new species, and that it was probably the only one indigenous to these Islands; a new species, because of its morphology, lack of periodicity and the rarity of filariasis in the Philippines; the only indigenous one, because the previous descriptions of the filariæ observed in natives of these Islands contained nothing which would exclude the possibility that the observers might have been dealing with *Filaria philippinensis*.

When our preliminary communication regarding this parasite was written we had seen but one case of infection with it, but since then we have had the opportunity of studying four additional cases, all in natives of the Philippine Islands. To Doctor Albert L. Miller, contract surgeon,

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United States Army, we are indebted for the additional cases which he found while examining the blood of a company of Philippine Scouts at Imus, Cavite Province, with the view of determining how many of this company were infected with *Filaria philippinensis*. These men, who were transferred to us for observation, belonged to one company of Scouts and all were born upon the Island of Luzon, in the Province of Ambos Camarines.

From a study of these cases we have been able to confirm our original description of this filaria and to make additional observations upon its morphology and life history, especially as regards its developmental changes within a mosquito, *Culex fatigans* Wied.

RÉSUMÉ OF THE ORIGINAL DESCRIPTION.

In order that the observations which follow may clearly be understood the following brief résumé of our original description is necessary:

Filaria philippinensis is a small blood filaria found in natives of the Philippine Islands; it presents no periodicity, occurring in practically equal, but small numbers, at all hours of the day and night; it is actively motile, possessing both lashing and progressive motion and presents for description a sheath, an anterior extremity, a body and a posterior extremity. The average length of the living filaria is 0.32 millimeter, but variations occur between 0.29 and 0.335 millimeter.

The sheath is visible at either extremity, being invisible along the rest of the body; it has the appearance of a fine thread, as thin as the flagellum of a trypanosoma; along the body the sheath is transparent and very tightly fitting, thus preventing the filaria from slipping backward and forward within it, as in the case of *Filaria nocturna* Manson and *Filaria diurna* Manson.

The anterior extremity or head consists of a hemispherical base, in the center of which is placed a small spicule which retracts within this base; surrounding this portion of the head is a serrated prepuce which, when closed, covers it, when retracted, exposes it; the number of serrations or lips can not be determined. The prepuce is constantly drawn back and forth, as is likewise the spicule, but the motion of the two is not always synchronous.

The body is graceful and sinuous, consisting of an outer, radially striated, musculo-cutaneous coat and an inner portion or body cavity; the latter is clear and refractile and contains the following constant viscera:

(*a*) *Anterior V spot.*—A bright, refractile, triangular area, placed at one side of the worm, about 0.105 millimeter from the anterior margin of the head, and opening by its apex upon the surface, piercing the musculo-cutaneous coat.

(*b*) *Central viscus.*—In the posterior portion of the central third of the body is situated a convoluted or spiral tube or cylinder, resembling a vine tendril, and presenting five or six spiral turns which progressively grow smaller, ending in a fine, curved or straight extremity. This central viscus is placed in the same portion of the worm as is the "granular mass" in *Filaria nocturna*.

(*c*) *Posterior V spot and papilla.*—At the center of the posterior third of the body there is situated a triangular spot, its apex opening upon the surface, piercing the musculo-cutaneous coat, where it marks the site of a distinct papilla which bulges beyond the body line and may represent the anus or cloaca of the adult worm.

The posterior extremity or tail, at a point midway between the posterior V

spot and the tip becomes suddenly attenuated to three quarters of its former diameter, thus forming a distinct offset upon each side; from this point the tail diminishes progressively and uniformly to a very fine, thread-like point. Because of its situation in relation to the embryonic anus and its apparently less vital characteristics, the portion of the tail beyond the attenuation probably dies or is sloughed off during the later development of the filaria.

In stained specimens, a column of deeply stained nuclei is observed running the entire length of the worm, broken here and there by unstained areas, which vary in position in individual specimens; the only "gap" in the stained column that is at all constant is situated at a point 20 per cent of the total length of the worm from the head; however, many specimens do not show this "gap," and there is also much variation in its situation in individual filaria. We do not regard it as of any diagnostic importance. In the stained specimen the anterior V spot, the central viscus, and the posterior V spot are not seen.

Filaria philippinensis is very actively motile, the movements being of a wriggling, lashing character and not progressive, as a rule, but at times a marked progressive motion is observed. (See figs. 1 and 18.)

LATER OBSERVATIONS.

The study of four more cases of infection with *Filaria philippinensis* has enabled us to add somewhat to the above description as regards the morphology, motility, and periodicity of this filaria.

Morphology.—We can add but little to our original description as regards the morphology of *Filaria philippinensis.* We have examined a very large number of filariæ in the blood with special reference to the armature of the head, but we have been unable to distinguish any definite number of lips; the spicule, mounted upon a smooth, hemispherical base, into which it retracts, is easily distinguished, but the retractile prepuce which incloses it can not be separated into definite lips, its margin being so very finely serrated. The serrations can easily be seen in the fresh specimen, but their number can not be determined, while in the stained specimen they are not visible.

In a certain proportion of stained filariæ in blood obtained from the mosquito's stomach shortly after the insect has bitten, and in which the sheath has been lost, what appears to be two lips can be seen, an upper one, broad and fleshy, and a lower, more slender and delicate. However, we are not convinced that these represent true lips, for the appearance may be due to the staining method, but their presence in a comparatively large number of the filariæ is suggestive.

The sheath, as we have already stated, is tight and generally only seen as a thread-like flagellum at the extremities of the worm. When the filaria is moving forward, the anterior end of the sheath bends backward along the side of the body, while the posterior end is lashed about by the movement of the tail; when the movements of the worm are lashing and not progressive, both ends of the sheath are whipped freely about. The filaria is never seen to slide forward and backward within the sheath,

this being impossible because of the closeness with which it envelops the body. In very rare instances in the fresh specimen, the sheath may be seen to be flattened out, having a ribbon-like appearance, but even when this occurs the filaria does not enter the flattened portion projecting at either extremity.

We are not able to add anything to our previous description of the anterior V spot, the central viscus, the posterior V spot or the tail of the worm as observed in the blood of man; the same is true of the measurements of the filaria as given by us and the morphology of the stained specimen.

Motility.—In our original description we stated that *Filaria philippinensis* possessed two forms of motility, one lashing but not progressive, which is most frequently observed; the other, a marked progressive motion occurring but rarely. In our examinations of the filariæ in our additional cases we have given special attention to the character of the movements exhibited by them and have found that progressive motion is much more common in fresh blood specimens than we at first supposed to be the case. We have found that in thick blood smears progressive motion occurs very frequently, if not as a rule, and we have also observed it in very thin smears; when it takes place the movement is serpentine in character, the head advancing through the surrounding masses of blood corpuscles with considerable rapidity. In a fairly thick smear, in one instance, a filaria in three minutes crossed four 18-millimeter ($\frac{3}{4}$-inch) microscopic fields in almost a straight line; in another case, eight 18-millimeter ($\frac{3}{4}$-inch) fields were traversed in half a minute; in a blood smear in which the cells were arranged in a single layer a filaria crossed a 18-millimeter ($\frac{3}{4}$-inch) field in one minute and six 4.25-millimeter ($\frac{1}{6}$-inch) fields in three minutes. Even when a portion of the specimen was reached in which the blood cells were in very small numbers, or indeed absent, the filaria did not show entire loss of progressive motion, although such clear spaces caused a temporary cessation; in such instances, after a few moments of twisting and turning, the head of the parasite would shoot forward and the progressive motion be resumed; in this way we have seen a filaria traverse four such open spaces in a specimen of blood and in each instance as soon as it reached the intervening clumps of blood corpuscles the progressive motion became more rapid and regular in character. At times the tail end advanced but this was invariably followed almost immediately by a propulsive effort of the tail which pushed the head and body forward for a considerable distance, after which the head continued its advance. In one specimen we observed progressive motion of filariæ for two hours after the blood was collected.

It should be remembered that the movements, both lashing and progressive, which have been described occur while the filaria is still inclosed within its sheath, progressive motion being unimpeded by the latter.

Periodicity.—Filaria philippinensis presents no periodicity as regards the time of its appearance in the peripheral blood or the number of embryos present at any one time. We have made extensive observations regarding periodicity in all five cases of infection with this filaria and can state conclusively that it can be found in the peripheral blood at all hours of the day and night and in practically the same numbers at all hours. The following table, which gives the results of examinations made every three hours during the twenty-four, demonstrates the lack of periodicity in *Filaria philippinensis:*

Case number 1.

Number in individual counts.	*Average per day and night.*
7 a. m., 3 filariæ in 3 blood smears.	
10 a. m., 2 filariæ in 3 blood smears.	
1 p. m., 2 filariæ in 3 blood smears.	7 a. m. to 7 p. m., 8 filariæ in 12 smears.
4 p. m., 1 filaria in 3 blood smears.	
7 p. m., 2 filariæ in 3 blood smears.	7 p. m. to 7 a. m., 8 filariæ in 13 smears.
10 p. m., 1 filaria in 3 blood smears.	
1 a. m., 3 filariæ in 4 blood smears.	
4 a. m., 2 filariæ in 3 blood smears.	

Case number 2.

Number in individual counts.	*Average per day and night.*
7 a. m., 5 filariæ in 3 blood smears.	
10 a. m., 1 filaria in 4 blood smears.	
1 p. m., 1 filaria in 3 blood smears.	7 a. m. to 7 p. m., 8 filariæ in 13 smears.
4 p. m., 1 filaria in 3 blood smears.	
7 p. m., 2 filariæ in 3 blood smears.	7 p. m. to 7 a. m., 8 filariæ in 13 smears.
10 p. m., 3 filariæ in 3 blood smears.	
1 a. m., 0 filaria in 3 blood smears.	
4 a. m., 3 filariæ in 4 blood smears.	

Case number 3.

Number in individual counts.	*Average per day and night.*
7 a. m., 2 filariæ in 3 blood smears.	
10 a. m., 1 filaria in 4 blood smears.	
1 p. m., 3 filariæ in 3 blood smears.	7 a. m. to 7 p. m., 8 filariæ in 3 smears.
4 p. m., 2 filariæ in 3 blood smears.	
7 p. m., 4 filariæ in 3 blood smears.	7 p. m. to 7 a. m., 10 filariæ in 13 smears.
10 p. m., 0 filaria in 3 blood smears.	
1 a. m., 5 filariæ in 4 blood smears.	
4 a. m., 1 filaria in 3 blood smears.	

A study of the above table will show that at no definite time during the twenty-four hours can the filariæ be said to be numerous enough to be characteristic of that time, and that no difference exists in the number observed in the peripheral blood during day and night. This fact, together with the presence of a sheath in *Filaria philippinensis,* serves to differentiate it from any other filaria which has been described as infecting man. It should be noted that it occurs in small numbers at all times

and this has been a prominent feature in all of our observations. It appears to us that this is a point of considerable diagnostic importance, for in all five of the cases practically the same number of filariæ was observed and that number was always a small one when compared with the immense quantities of *Filaria nocturna, Filaria diurna,* and *Filaria perstans* Manson which are commonly found in cases infected by the last three organisms.

Pathogenicity.—In none of the cases did we observe any symptoms or pathological lesions which we could feel justified in considering as being due to the presence of the filaria. As stated in our original communication, one patient had a history of having suffered from chyluria, but during the time he was under our observation he presented no symptoms; one man had a periostitis while under observation and one, amœbic dysentery. An examination of the fæces of three of the four Scouts demonstrated an interesting series of combined infections due to animal parasites. Of the three men, one had a combined infection with *Filaria philippinensis, Anchylostoma duodenalis* and *Trichocephalus dispar;* the second, with *Filaria philippinensis, Entamœba dysenteriæ, Anchylostoma duodenalis* and *Trichocephalus dispar,* and the third with *Filaria philippinensis* and *Anchylostoma duodenalis.*[2]

THE DEPELOPMENT OF FILARIA PHILIPPINENSIS WITHIN CULEX FATIGANS.

We have made numerous examinations of mosquitoes which were infected by biting patients who harbored embryos of *Filaria philippinensis,* most of the insects so infected being *Culex fatigans* Wied, some few being *Stegomyiæ.* In our examinations we have not found that the filariæ undergo any development in *Stegomyiæ,* and think it probable that they do not, for, while our observations on this point are not sufficiently numerous to justify us in making positive statements, it is asserted by Daniels that *Filaria nocturna* will not develop in *Stegomyia.*

However, in *Culex fatigans* Wied, we have been able to trace the complete development of the filaria up to the time that it becomes lodged in the mosquito's labium and is ready to infect the next person bitten by the insect. The stages of this development are well shown in the accompanying photomicrographs and in numerous camera-lucida drawings, and may be quite as well, or better, studied from them as from the written description which here follows:

One of the earliest observations to be made in studying infected mosquitoes is one relating to the number of filariæ ingested. In some manner, concerning which it is possible to construct interesting hypotheses, the mosquito manages to get from the body of the patient 40 to 50 or more

[2] In view of the recent finding by Lieutenant Clarence L. Cole, Medical Department, United States Army, of *Necator americanus,* in natives of these Islands, it is possible that our cases were infected with it, as the ova were not measured.

times as many filariæ as it is possible for us to obtain in a similar amount of blood from a needle prick. Thus, in good thick smears under 22-millimeter (⅞-inch) cover-glasses, we will usually find but one or two, and oftentimes no filariæ. In the blood from the stomach of a mosquito which has recently bitten, the amount of blood usually appears to be less than in these thick cover-slip preparations, but it is nearly always possible to find from 40 to 80 filariæ, and it has occurred to us that this fact might have a practical value in examining cases of suspected filariasis in which the parasites are so few in number as readily to be missed. It might be of use in revealing embryos in the blood of cases of elephantiasis, where the filariæ, though believed to be present, are seldom found. We have not had an opportunity to put our suggestion into practice except on our last four cases of known filariasis, in all of which the result has been as stated.

Once in the stomach of the mosquito, the filariæ continue their active motion, which is more uniformly progressive than in the fresh blood, for several hours (the exact length of time we are unable to state) until they discard their sheaths and pierce the stomach wall, entering the body cavity.

Stages of growth of Filaria philippinensis within Culex fatigans Wied.—It is necessary to state here that the various stages of growth are not passed through in uniform intervals of time but that the periods mentioned below, as well as the measurements given, are thought merely to represent averages. Thus, embryos free from their sheaths may be found in the tissues outside of the stomach, while others ingested at the same time are still struggling in the stomach to free themselves. Likewise, at the eighth day we have, in a heavily infected mosquito, seen some filariæ which appeared to have undergone fully twice as great a degree of development as others, although we knew that they had all been ingested at one feeding.

This preliminary being understood, we may say that in twenty-four hours after ingestion by the mosquito the filariæ have escaped from their sheaths and pierced the stomach wall, being found free in the abdominal cavity. Here they are sluggish in motion, unchanged as to size, but have a more granular appearance. The V spots may often still be distinguished, but the central viscus can not. It is not uncommon to find some of these worms dead and we think that the mortality among them is high at all stages of their development, but more particularly so during the early ones. It is unusual to find more than four or six filariæ which undergo the complete cycle of development within the mosquito at one time, while on the other hand only one may remain, and most frequently none are to be observed in the mosquito at the end of ten days or two weeks. Once we encountered fifty-one filariæ in a mosquito's thorax on the eighth day, but we have in no other instance found anything like these numbers after the second.

By the third day, possibly earlier at times, the filariæ have left the abdominal cavity and are to be seen among the thoracic muscles of the mosquito, where they show very sluggish motion and are observed to have undergone a very marked change in morphology.

The length has decreased from 0.32 to 0.21 millimeter; the breadth has increased from 0.0065 to 0.01 millimeter; all parts of the body have participated in the increase in width except the tip of the tail—that is, the part of the tail back of the sudden diminution described in our first paper. This part has not enlarged in size, and, as will be seen, it disappears at a later period, thus fulfilling the prediction concerning it which we made in our first publication. The posterior V spot is still visible and is manifestly increased in size. The body presents a granular appearance and the central viscus has disappeared. (See figs. 2, 3, 19, and 20.)

At the end of six days the filariæ are still as short as at three days, but they have undergone a further increase in breadth which at this stage varies from 0.014 millimeter near the anterior end to 0.027 millimeter near the posterior, the average being about 0.02 millimeter. The tip of the tail is still present and still unenlarged and now presents a "pigtail-like" appearance in its attachment to the more bulky body. The latter still has a granular aspect but some cell structure can be made out and the alimentary canal outlined. The posterior V spot, as such, has disappeared, but its place is occupied by a rudimentary anus. The motion of the worm is still sluggish, being about the same as it is at the third day. (See figs. 4, 5, and 21.)

On the eighth day we find the filaria increased in length and in breadth; the "pigtail" portion of the tail in most instances, though not in all, has disappeared; the alimentary canal can be traced the whole length of the worm. The length averages about 0.6 millimeter, the breadth 0.035 millimeter; motion is sluggish but the filaria is possibly a little more active than it was at the sixth day. (See fig. 22.)

From the eighth to the eleventh day the worm undergoes a more rapid development than in any other similar period and at the expiration of this time is found to have attained a length of from 1.2 to 1.6 millimeters and a width varying from 0.04 down to 0.02 millimeter, the width being less in the longer worms. (See figs. 6, 7, 8, and 23.)

Some worms at this time show as complete a development as we have ever seen and apparently have no other change to undergo except the lengthening and narrowing, a change of form rather than of size, necessary to enable them to enter the labium. The head is truncated, the mouth a terminal, crater-like, circular opening, forming the base of a conical cavity; no lips are visible. Nothing recognizable as the analogue of the anterior V spot is distinguishable. The intestinal canal is well

developed, the œsophagus straight and broad, the intestine narrower and much coiled, particularly at a point corresponding in situation to that of the spiral viscus in the blood embryo. The anus is a slit, directed from within outward and backward (see fig. 17); the intestine, apparently, does not terminate at the anus but continues to the end of the body. The tail is tipped with three well-defined papillæ; this number is probably constant, although only two are usually visible in profile.

By the eleventh or twelfth day some of the filariæ may be found in the mosquito's head, by the fourteenth or fifteenth they are encountered in the labium, having completed their development in the insect, so far as we have been able to observe. At this stage the filariæ are found within the labium, the fleshy underlip of the insect, where they lie side by side, with their heads directed toward the labella. We have observed as many as four within the labium, and it is probable that as a rule they occur in this situation in pairs. (See figs. 13, 14, 15, and 16.)

As our work has been done by teasing preparations and not by sectioning, we are unable to state exactly where the filariæ lie in the head or how they get into the labium. However, the fact that they do reach that situation is beautifully illustrated in the photomicrographs, which show a fragment of the labium with the tails of the filariæ protruding from the proximal end. This preparation was made on the sixteenth day after the mosquito had bitten the filariasis patient.

The worm, at this stage, has diminished markedly in breadth, the average measurement for this dimension being not more than 0.02 millimeter, while individuals have been measured in which it was only 0.015 millimeter. The former figure, however, applies in most instances. The length varies greatly and we have measured specimens which range from 1.236 to 2.20 millimeters. We can say from our observations that the worm when found in the mosquito's labium may average 1.8 millimeters in length, but that others in the same situation and in the same mosquito, actively motile and apparently ready to pass to another host, may be as short as 1.24 or 1.27 millimeters. Two worms taken from the mosquito's head upon the eleventh day gave 1.496 and 1.630 millimeters, respectively, and this variation in length is noticed in individual worms after the very earliest stages in the mosquito. We have thought that the long and short groups may represent the sexes, but have no other evidence to offer in support of such a supposition. (See figs. 10, 11, 24, and 25.)

At this stage of development the alimentary tract is well defined and extends from the mouth to the anus, which is well marked; it possesses some strength, as is shown in fig. 9, which represents a worm broken by the attempts made to dissect it from the labium. Here the fragments are held together by the intact cellular tube forming the intestinal canal. The anus is well developed and is easily seen, presenting the same appearance as it does at the eleventh day of development.

Another point easily determined at this time is that the post-anal papillæ are three in number. Annett, Dutton, and Elliot state that

Filaria nocturna has four of these papillæ and we have carefully looked for four on this filaria. There is no difficulty in making out three in *Filaria philippinensis,* but in no instance have we seen four. When the end of the tail is facing the observer it will be seen that the three papillæ are arranged in a triangular manner and are apparently curved inward. (See figs. 12 and 26.)

In most spicimens an appearance suggestive of two narrow tubes, running in general parallel with the alimentary canal, one on either side, may be seen. These tubes we think probably represent the future generative organs, but we are unwilling to make positive statement either as to their constant presence or their significance. They, or certain masses of cells extend posteriorly to the anus, apparently clear back to the terminal knobs or papillæ, and in at least one specimen their terminations appeared to constitute the papillæ.

Some of the filariæ from the head and labium are very actively motile; others show no motion, but as these presented no evidence of degeneration we think that they were probably killed by the chloroform used in destroying the mosquitoes.

The following table gives the principal differential features between the embryos of *Filaria philippinensis* and of other known filariæ, as they occur in the blood of man:

Name.	Length.	Breadth.	Sheath.	Head.	Tail.	Anterior V spot.
	mm.	*mm.*				
F. philippinensis sp. nov.	0.32	0.0065	Present, tight.	Serrated retractile band and spicule.	Pointed, abruptly attenuated.	Present.
F. nocturna Manson.	0.30	0.0075	Present, loose.	Six lips	Pointed	Do.
F. diurna Manson.	0.30	0.0075	do	do	do	Do.
F. perstans Manson.	0.20	0.0045	Absent	Retractile fang	Blunt	Do.
F. demarquayi Manson.	0.20	0.005	do	Spine	Pointed	Do.
F. ozzardi Manson.	0.21	0.0051	do	(?)	do	Absent.
F. magalhaesi R. Blanchard.	0.33	0.005	do	Unarmed	do	Do.
F. volvulus Leuckart.	0.30	0.005	do	Rounded	do	Present.
F. tanaguchii Tan.	0.295	0.007	do	Blunt	do	Absent.
F. ? (*Tanaguchii*)	0.164	0.008	Present	do	Conical	Do.
F. gigas Prout	Much longer and thicker than any of the above.		Absent	(?)	Blunt	(?)

Name.	Central viscus.	Posterior V spot.	Movement.	Periodicity.	Adult.
F. philippinensis sp. nov.	A spiral tube or cylinder.	Present; also a papilla.	Lashing and progressive.	None	Not found.
F. nocturna Manson.	Granular mass.	Present	Lashing	Nocturnal	*F. bancrofti.*
F. diurna Manson.	Absent	do	do	Diurnal	Not found.
F. perstans Manson.	do	Absent	Lashing and progressive.	None	*F. perstans.*
F. demarquayi Manson.	(?)	(?)	Progressive	do	*F. demarquayi.*
F. ozzardi Manson.	Absent	Absent	do	do	*F. ozzardi.*
F. magalhaesi R. Blanchard.	do	do	(?)	(?)	*F. magalhaesi.*
F. volvolus Leuckart.	do	do	(?)	(?)	*F. volvolus.*
F. tanaguchii Tan.	Granular streak from mouth to tail.	do	Progressive	None	*F. taniguchii.*
F.? (*Tanaguchii*)	Absent	do	Lashing	(?)	Not found.
F. gigas Prout	(?)	(?)	(?)	(?)	Do.

CONCLUSION.

Briefly summarized, the history of the development of *Filaria philippinensis* within the mosquito, *Culex fatigans* Wied., is as follows: In from fourteen to fifteen days the development is complete and the filaria has passed into the labium of the mosquito; the sheath of the embryo is lost in the stomach, and the worm then penetrates the stomach wall and reaches the muscles of the thorax where most of the developmental changes occur; during this period of time the filaria has increased in length from 0.32 millimeter to as much as 2.20 millimeters, and in breadth from 0.0065 to 0.02 millimeter; it has developed a well-marked intestinal canal, divided into oesophagus and intestine, a well-defined anus and three papillæ which are situated at the end of the tail; the mouth appears to be simply a circular cavity having no distinct lips. Development so far as the morphology of the worm indicates, appears to be complete at about the eleventh day, the only changes occurring after that being a lengthening and narrowing of the filaria, which enables it to enter the labium of the mosquito.

In concluding, we desire to express our appreciation of the assistance given us by Mr. Charles S. Banks, entomologist of the Biological Laboratory, Bureau of Science, and Mr. Charles Martin, photographer of the Bureau of Science.

ILLUSTRATIONS.

PLATE I.

FIG. 1. *Filaria philippinensis* in freshly drawn blood.
2. *Filaria philippinensis* three days in *C. fatigans*. × 115.
3. *Filaria philippinensis* three days in *C. fatigans*. × 229.

PLATE II.

FIG. 4. *Filaria philippinensis* six days in *C. fatigans*. × 92.
5. *Filaria philippinensis* six days in *C. fatigans*. × 206.
6. *Filaria philippinensis* eleven days in *C. fatigans*. × 76.
7. Tail of *Filaria philippinensis* eleven days in *C. fatigans*. × 183.

PLATE III.

FIG. 8. Head of *Filaria philippinensis* eleven days in *C. fatigans*. × 275.
9. Broken *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 115. Showing strength of alimentary canal.
10. *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 115. Showing elongation and narrowing in labium.

PLATE IV.

FIG. 11. *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 220. Showing alimentary canal. A portion of the alimentary canal has been extruded by pressure.
12. Tail of *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 275. Showing three papillæ.
13. *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 92. In labium.
14. *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 220. In labium.
15. *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 86. In labium.

PLATE V.

FIG. 16. *Filaria philippinensis* fifteen and one-half days in *C. fatigans*. × 240. In labium.
17. *Filaria philippinensis* eleven days in *C. fatigans*, showing anus.

PLATE VI.

FIG. 18. *Filaria philippinensis* in freshly drawn blood. Killed and drawn by the aid of camera-lucida at once. × 330.
19. *Filaria philippinensis* in stomach of *C. fatigans* six to twelve hours after ingestion. Sheath discarded. × 330.

20. *Filaria philippinensis* in thorax of *C. fatigans* three days after ingestion. Note size of worm and size of post V spot. × 330.
21. *Filaria philippinensis* in thorax of *C. fatigans* six days after ingestion. Note part of contents extruded through V spot. × 330.
22. *Filaria philippinensis* in thorax eight days after ingestion. × 63 and × 330.

PLATE VII.

FIG. 23. *Filaria philippinensis* in thorax eleven days after ingestion. × 63 and × 330.
24. *Filaria philippinensis* in labium fifteen and one-half days after ingestion. × 63 and 330.
25. *Filaria philippinensis* in labium fifteen and one-half days after ingestion. × 63 and 330.
26. *Filaria philippinensis* in labium fifteen and one-half days after ingestion. × 63 and 330.

Note. In Figs. 22 to 26, the entire filaria is represented at A, the tail at B and the head at C.

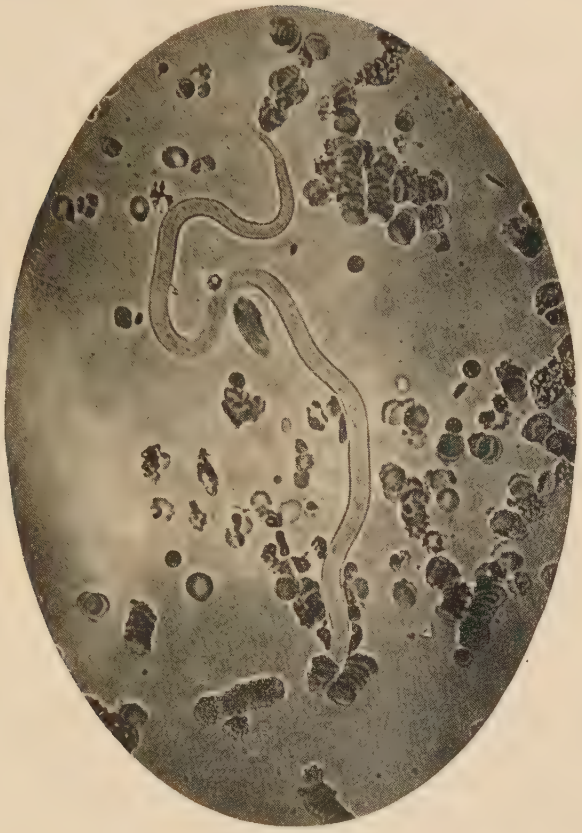


FIG. 1.

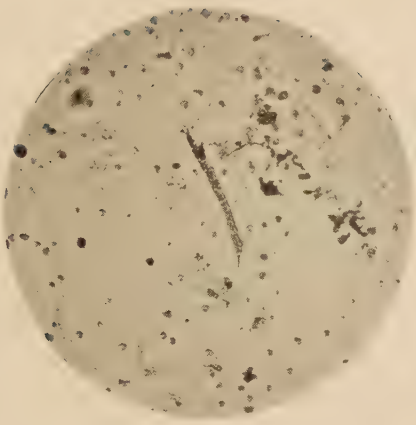


FIG. 2.

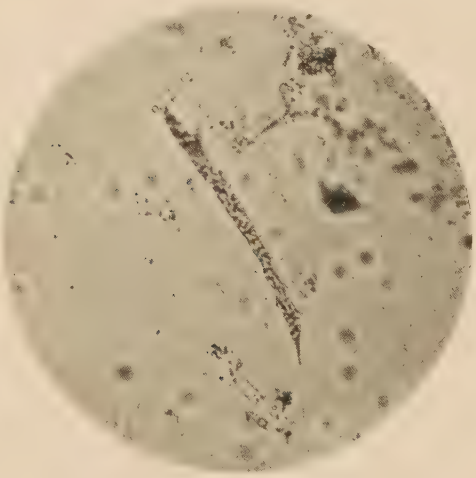


FIG. 3.

PLATE I.

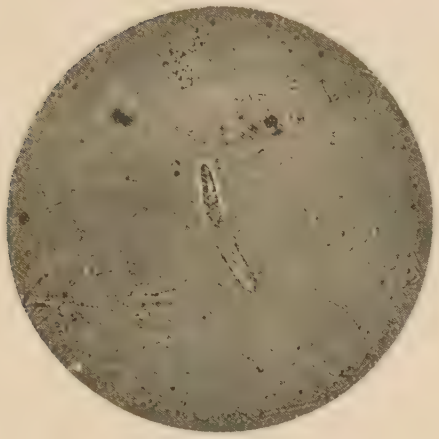


FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.

PLATE II.

FIG. 8.

FIG. 10.

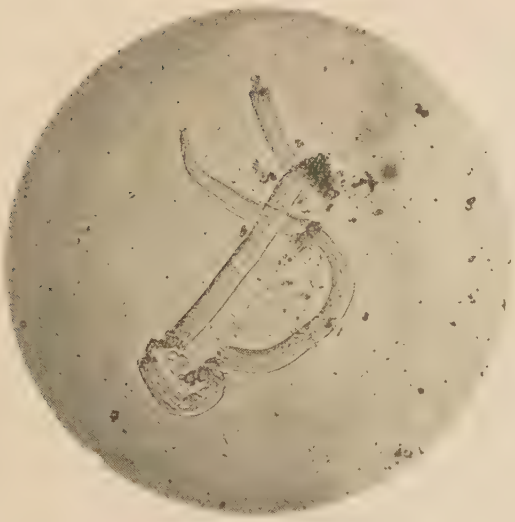


FIG. 9.

PLATE III.

FIG. 11.

FIG. 13.

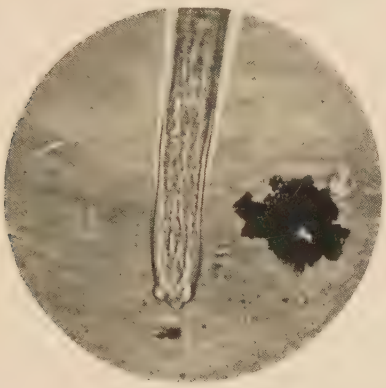


FIG. 12.

FIG. 14.

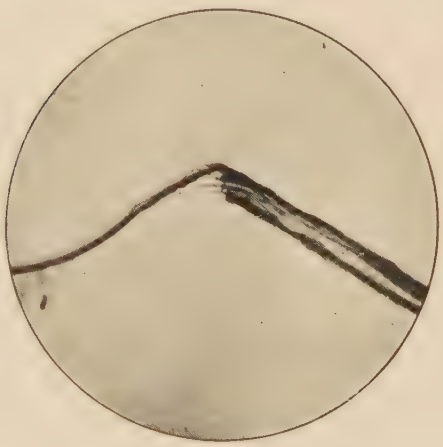


FIG. 15.

PLATE IV.

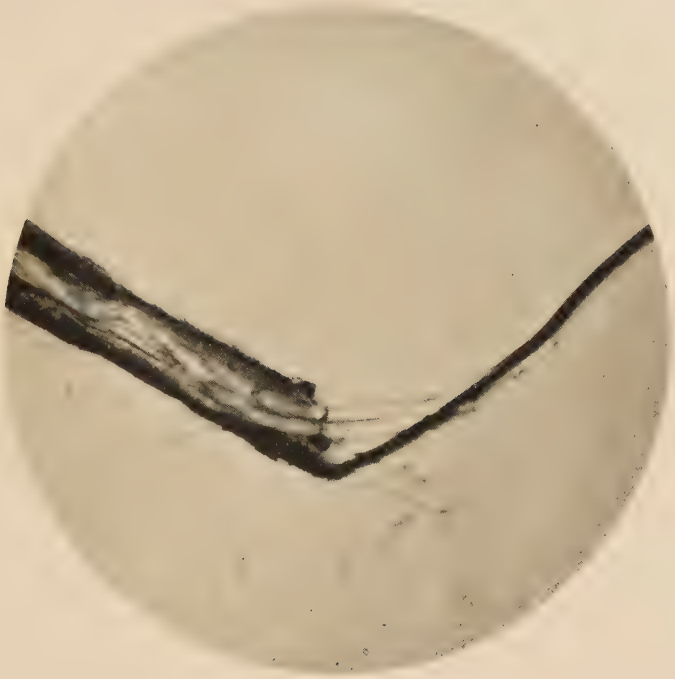
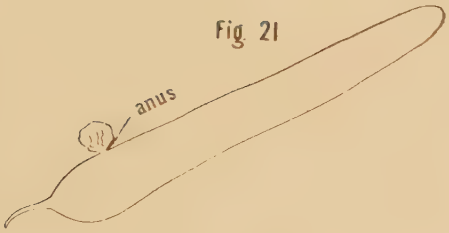
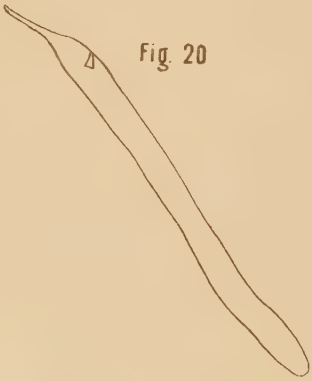


FIG. 16.

FIG. 17.

PLATE V.





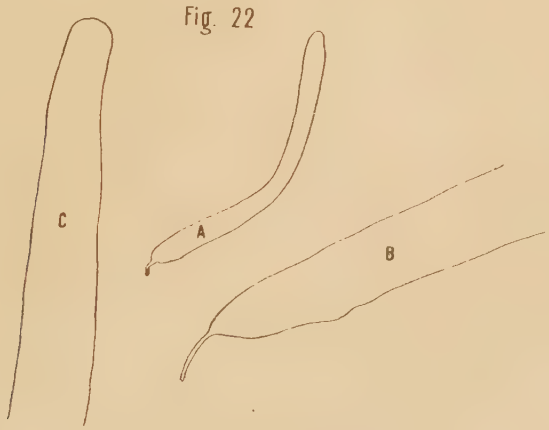


PLATE VI.

Fig. 23

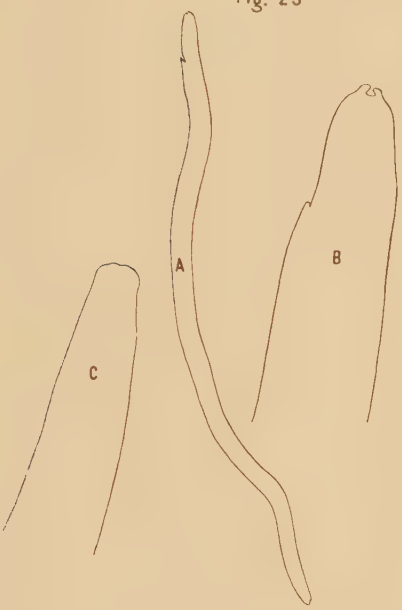


Fig. 24

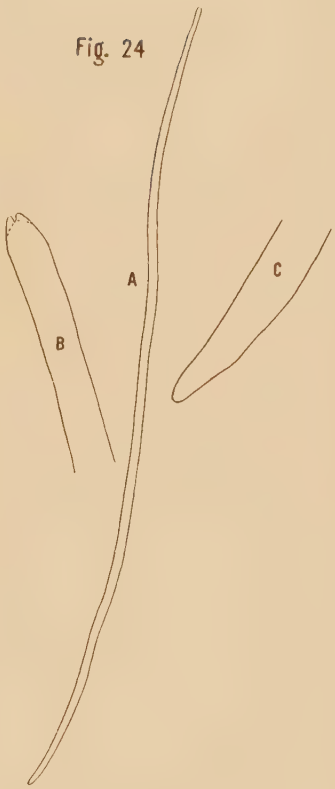


Fig. 25

Fig. 26

PLATE VII.

PARAGONIMIASIS IN THE PHILIPPINE ISLANDS.

By W. E. Musgrave.
(*From the Biological Laboratory, Bureau of Science.*)

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I. INTRODUCTION.

Trematode infections, next to the protozoan diseases, are the most important parasitic conditions which must be met by medical men in the Philippine Islands.

The order *Malacocotylea* is a very large one, containing many species, but of these only a comparatively small number are known to infect man; those which are parasitic for human beings, compiled from Stiles's publication, are shown in Table No. 1, page 31. They represent 4 families, 10 genera or collective groups, and 15 species. Of this number only about 8 species are sufficiently common in man to be of great

importance. All flukes are considered to be disease producers, regardless of the stage of the life cycle of the parasite or of the nature of the host in which they are found. The adult parasites with a very few exceptions, whether in man or other animals, are found only in diseased tissues, and the miracidia and cercaria may produce disease of snails and other hosts in which they may be living.

So far as I have been able to determine, only two cases of trematode infection have previously been reported from the Philippine Islands. One of these was a case of infection with *Opisthorchis sinensis* Cobbold, reported by Dr. Mallory at the last annual meeting of the Philippine Islands Medical Association, in which the diagnosis of the egg was made by Dr. Strong; the other was one of schistosomiasis by Dr. Woolley.

The following paper is the first of a series to be published during the year on material which is already available, as follows:

One case of infection with *Opisthorchis noverca* (?) Braun, in a Chinaman; 2 cases with autopsies, in which the infecting flukes, though not thoroughly identified, are probably *Fasciola gigantica* Cobbold and *F. hepatica* Linn., respectively; 8 cases infected with *Schistosoma japonicum* Katsurada, with 2 autopsies; 18 with *Opisthorchis sinensis* Cobbold, with 1 autopsy, and 17 with *Paragonimus westermanii* Kerb., with 8 autopsies; the total being 46 cases in human beings. I have also studied quite a large series of infections in the lower animals.

These reports appear in monographic form because the observations have included too many points, not only about the parasites but also particularly about the diseases caused by them, to allow of a satisfactory presentation of the findings in any other manner.

I wish to express my thanks to Dr. Edwin C. Shattuck, resident physician to Bilibid Prison, for many courtesies and much assistance in the observations on the clinical material, much of which is from his service.

II. DEFINITION.

Paragonimiasis is a chronic or subacute, general or local infection, with a species of the genus *Paragonimus,* only one species of which genus, *P. westermanii,* is known to infect man. The disease is characterized anatomically by the production of peculiar, bluish, slate-colored, necrotic, cystic lesions with rather dense, fibrous walls which contain a material resembling anchovy sauce and usually, but not always, the eggs or adult *Paragonimus.* Other types of lesions are often present and many different organs may be involved. The most frequent are bronchopneumonia and bronchiectasis; cystic abscess of the brain, spleen, omentum, pancreas, muscles, lymphatic glands, and skin; and infiltration, ulceration, and abscess formation in the intestine.

The symptomatology in general is that of a chronic inflammatory

process, and special clinical manifestations are due to the involvement of special organs which give rise to such symptoms as cough, hæmoptysis, pleuritic pains, diarrhœa and abdominal soreness. The life history of the parasite and the exact mode of infection by it are not known.

III. NOMENCLATURE.

A. SYNONYMS.

The following may be mentioned among the many names by which this disease has been known: Parasitical hæmoptysis, parasitic hæmoptysis gregarinosis pulmonis, pulmonary distomatosis, pulmonary distomiasis, endemic hæmoptysis, and paragonimiasis. Parasitical hæmoptysis is the most extensively used of these terms and at the time of its introduction it answered very well, since formerly the distribution of the parasites throughout the body was regarded as limited and it was not known that such extensive infection existed as has recently been described.

All of these names, except paragonimiasis, are objectionable because none of them are accurate, specific or definite, and their number leads to a confusion which can only be overcome by the adoption of a term which fulfills all the requirements of nomenclature. Paragonimiasis is such a name. It is in line with modern nomenclature in parasitic infections and is applicable to all types of the diseases, whether they are found in man or in animals.

This term was introduced by Stiles and Hassall and has been adopted by Mense in his new Handbook of Tropical Medicine. It is the only name for the infection which will be used in this report and, owing to the extensive distribution of the parasite in man and the consequent logical variation in symptomatology, I shall recognize the following types of the disease in their appropriate places: General paragonimiasis, thoracic or pulmonary paragonimiasis, cerebral paragonimiasis, and abdominal paragonimiasis.

IV. BRIEF HISTORY.

A. GENERAL.

Paragonimus westermanii was discovered by Kerbert in 1878 in the lungs of a royal Bengal tiger and was by him named *Distoma westermanii*. In 1879 Ringer found the parasites in a native of Formosa. Cobbold (1880) named the parasite *Distoma ringeri*.

Baelz (1880), who was working in Japan, introduced the name *parasitic hæmoptysis* (*parasitäre hämoptoë*) for the disease and discussed the parasite under the designations *Gregarina pulmonum* and *Gregarina fusca;* he further used *gregarinosis pulmonum* as a synonym for the disease. Baelz gave further valuable contributions on the subject in 1883 and 1901. In 1883 he adopted the name *Distoma pulmonale* for the parasite

Suga (1881) found the infection in man in Japan, and in 1883 described the parasite as *Distomum pulmonis*.

Manson made valuable original contributions to the subject in 1881, 1883, 1889, and 1893. He proposed *parasitical hæmoptysis* and *endemic hæmoptysis* as names for the disease and designated the parasite as *Distoma ringeri* and *Distoma pulmonale*. Further information of value has been furnished by Taylor (1884), Leuckart (1889), Yamagiwa (1890 and 1892), Stiles (1894, 1901, and 1904), Stiles and Hassall (1900), Ward (1893 and 1895), Katsurada (1898 and 1900), Miura (1889), and by a number of Japanese writers whose articles are not available. Prominent among these are Otani, Taniguchi, Majima, Miyake, and Matsui.

The landmarks in the history of this parasite and the diseases caused by it are as follows:

The discovery of the parasite by Kerbert (1878); the discovery of the parasite in human beings by Ringer (1879); the establishment of the relation of the parasite to the disease in man by Suga, Baelz, and Manson; the discovery of the more extensive distribution of the parasite and its location in the brain, producing Jacksonian epilepsy, by Otani and Yamagiwa; its discovery in the eye and lids by Taniguchi, Miyake, and Matsui; the establishment of the zoölogical position of the parasite by Stiles and Looss; the discovery of the infection in various animals, i. e., in the tiger by Kerbert, 1878; the cat by Ward, 1894; the dog by Railliet, 1890, and the hog by Stiles, 1899; the discovery of the parasite in the United States by Ward, and the elucidation of the pathology and symptomatology of the disease by Manson, Baelz, Miura, and Katsurada.

B. IN THE PHILIPPINE ISLANDS.

Because of the geographic position of the Archipelago and the close commercial and social intercourse between these Islands and Japan and China, it has repeatedly been predicted that fluke infections would be found here. Notwithstanding this expectation and the large amount of clinical and anatomical work which has been done in the Philippines, this is the first report of infections with *P. westermanii* Kerb. in the Archipelago, either occurring in natives or foreigners. As was mentioned in the introduction, there have been but two previous reports, of infection by trematodes of any species in the Philippine Islands, these being of single cases, one of *opisthorchiasis* and the other of *schistosomiasis*.

I encountered my first case of paragonimiasis early in 1906 and since that time have seen 16 others. The discovery of this number of cases in less than one year by one observer does not, in my opinion, indicate any exacerbation of the infection nor any change in the class of available material, but is due to a closer observation and study of that which is at hand. Since becoming interested in this class of diseases and

familiar with the appearance of the various lesions, I am confident that similar material has passed through my hands unrecognized many times during the last seven years, and identical experiences have probably occured with others. It may safely be stated, to judge from the wide local distribution of my cases, that trematode infections are fairly common among the natives of these Islands and that the infection has been endemic here for many years.

V. MATERIAL.

The material upon which this report is based consists of 17 cases with 8 autopsies. Abstracts from the protocols follow and the summaries of the findings and the analyses of the lesions and symptoms will be taken up under the appropriate headings furnished in the outline.

Case No. 1 (30918).—Paragonimiasis and amœbiasis of the lungs, pleuræ, diaphragm, omentum, peritoneum, spleen, liver, intestine, lymphatics, prostate, bladder and abdominal wall; death; autopsy.

The patient, a Filipino prisoner, was under observation in hospital for one week, suffering with high fever, 30° to 40°, severe cough, pains in the chest, and some dyspnœa. There was severe head-ache, mild delirium at times and insomnia. The bowels were constipated, the abdominal wall rigid, and tenderness was complained of over the entire abdomen. A blood examination showed nothing abnormal except a moderate polymorphonuclear leucocytosis. The sputum was negative for tubercle bacilli, but on the morning before death a few trematode eggs were found. The stool contained many amœbæ, blood cells, and mucus and a few eggs similar to those in the sputum.

Autopsy two hours after death: Emaciation and anæmia marked, severe conjunctivitis of left eye; old, bluish-colored ulcer in the right axilla, which on section connects with broken-down lymphatic glands. The eggs of *P. westermanii* are found in this ulcer. The superficial lymphatics are all moderately enlarged and those in the groins markedly so, and this enlarged chain extends down into Scarpa's triangle. The scrotum is enlarged and on section the epididymis contains *Paragonimus* cysts which apparently are continuous through the inguinal canal to the abdominal cavity.

The *subcutaneous tissue* is scanty and dry, the muscles soft, pale and coarse. A small *Paragonimus* cyst is observed in the left pectoralis major and another in the abdominal wall just above the symphisis. Upon opening the chest a number of the small bluish *Paragonimus* cysts are found on the under surface of the sternum and on the exposed pleuræ and pericardial membranes. Both *pleural cavities* contain a considerable quantity of fluid, filled with stringy masses and flocculi which settle to the bottom upon standing. The *pleuræ*, particularly the visceral layers, are much thickened. The pleural surfaces are covered with many of the cysts and even external to the parietal pleuræ these lesions are found. There are several small areas of chronic obliterative pleuritis and *Paragonimus* lesions are numerous in the fibrous tissue forming the adhesions. Both *lungs* show a moderate bronchitis, particularly of the larger tubes, but no eggs or parasites are found in the bronchi and no definite bronchiectatic cavities can be located. There are numerous areas of bronchopneumonia throughout both lungs, the largest near the pleural surfaces; many of these pneumonic areas are not to be distinguished from such lesions in other diseases of bacterial origin, while others, on section, have a necrotic center containing material like anchovy sauce and often, but not

always, adult parasites or eggs of *P. westermanii*. In addition to these pneumonic areas, both lungs contain many of the typical bluish *Paragonimus* cysts from 0.005 to 0.01 in diameter.

The *pericardial cavity contains* a small amount of a slightly cloudy fluid. The serous surface is dull in appearance and slightly adherent over the right heart; showing through the visceral pericardium are a number of irregular, slightly brownish, granular appearing areas similar to those described in case No. 2 (see Pl. 1). Eggs are found in these areas but none in the pericardial fluid. The *heart* is of normal size and free from valvulitis or other marked organic change. The muscle is a little brown and coarse, but except just under the pericardium no gross lesions are seen.

The *abdominal cavity* presents a most striking picture, all visible tissues being matted together and studded with the bluish-colored *Paragonimus* cystic abscesses. In places where adhesions have been separated, for instance, between the bowel surfaces or omentum and the abdominal wall, an area of bluish color of equal size to the adhesions is left, and often small, necrotic areas with eggs and parasites are exposed. Everywhere there is a moderate, subacute peritonitis, light, dry, dirty-colored adhesions binding all the organs. Both the abdominal and pleural surfaces of the diaphragm contain many abscesses. Similar lesions are also found in the deeper structures of this organ.

The *spleen* shows some perisplenitis and at the points where this occurs superficial areas of infection with the parasites or eggs are visible. On section, a moderate increase in the soft pulp is seen but no other change can be observed.

The *liver* is of normal size but adherent to the abdominal wall, diaphragm, intestine and other structures; the perihepatitis being due to the action of *Paragonimus*. On section, the organ is soft and pale and contains many small abscesses from 2 millimeters to 10 millimeters in diameter. These abscesses closely resemble the multiple amœbic ones which are so often seen, but in others the color and contents more closely resemble the *Paragonimus* cysts. Microscopically, both amœbæ and *paragonimus* eggs are found in some of these abscesses. The gall bladder and ducts are large and distended with normal-appearing bile; no parasites or eggs found.

The *kidneys* are surrounded by many adhesions containing very many abscesses of the *Paragonimus* type. Some of the lesions are subcapsular and others are in the pelves of the kidneys and in the ureters. Both organs are somewhat increased in size, soft and œdematous.

The *bladder* wall contains numerous cysts and the prostate gland is also involved.

The *pancreas* shows a few cysts near its head, these being a direct infection from the adherent structures.

The *appendix* is bound down in a mass of adhesions and abscesses and its wall is involved in the parasitic processes. The abdominal lymphatics are mostly enlarged and soft, many containing characteristic abscesses with parasites and eggs.

The *omentum* is plastered to all the abdominal structures; it is thickened, œdematous, and studded with the typical bluish abscesses.

The *stomach* is not involved excepting at points of adhesion on its outer surface. The walls are free from abscesses, and nothing abnormal is noted on the mucous surface.

The *small intestine*, from near its upper end to the cæcum, is severely infected. The *Paragonimus* lesions involve all of its coats, and are most severe in the ileum and lower jejunum. The mucous surface shows typical cysts of various sizes, some standing out well into the lumen of the bowel; ulcers resulting from

broken down lesions are also present. The Peyer's patches are slighty swollen but appear to be free from the parasitic infection.

The *large bowel* in general presents a very similar picture to the small intestine, but in addition there is quite extensive amœbic ulceration extending from the cæcum to the rectum.

The *cerebro-spinal canal* was not opened.

Case No. 2 (31508).—Paragonimiasis, acute general infection, with death after eight days in the hospital; autopsy.

Nothing is known of the previous history of this patient beyond his statement that he had never been ill before. He was sick in hospital for about eight days before death with high fever, cough, and rapid, shallow respiration, abdominal pains and severe diarrhœa; he constantly complained of headache. The abdomen was moderately distended and exquisitely tender in the region of the gall bladder and over the descending colon. There was considerable difficulty in urination. Expectoration was abundant, and sometimes tinged with blood, but upon microscopic examination no tubercle bacilli or eggs were found in the sputum.

Autopsy four hours after death: The general nutrition is very good and slight jaundice of the conjunctivæ is visible. A macular skin eruption is noted over the lower extremities, abdomen, and flexor surfaces of arms. The muscles are soft and exceedingly pale. The pectoralis major muscles are very coarse, pale, and contain a number of small, dark spots about 1 to 3 millimeters in diameter. From one of these spots an adult *P. westermanii* was extracted. The *lymphatics* in the axilla are moderately enlarged and some of them congested.

The *left pleural cavity* contains about 750 cubic centimeters of a yellow, flocculent fluid with long, tenacious shreds of tissue. Both the visceral and parietal pleuræ are studded with raised, soft, dark-bluish colored, cystic abscess-like bodies which, on section, contain a reddish-brown granular matter. Scattered through the left lung are a number of areas of bronchopneumonia; on section most of these show one of the above-described cysts, surrounded by pneumonic areas, but in other instances the areas resemble those of ordinary bronchopneumonia. On the *right side* the general condition is similar to that on the left, but the lesions are much more extensive the entire lung being so completely filled with these pneumonic areas that it appears to be almost solid. There is marked bronchitis. Ova, but no parasites are found free in the bronchial secretion.

The *pericardial cavity* contains a small amount of normal-appearing fluid and both the visceral and parietal serous surfaces show bodies similar to those found in the pleural cavities. Over the surface of the heart itself (Pl. I) are many little, raised, brownish, granular bodies varying from 1 to 3 or 4 millimeters in diameter; these are somewhat hard, surrounded by congested zones and follow closely in their distribution that of the vessels. On section, the *heart muscle* is found to be very friable and pale, but it contains none of the bodies already mentioned. Both the upper and the lower surfaces of the *diaphragm* are studded with these small, dark, cyst-like bodies. The diaphragm itself is very much thickened and contains a number of abscesses within its substance.

The entire *abdominal cavity* is almost obliterated by a mass of adhesions, and dark, bluish cystic abscesses, varying in size from 1 millimeter to 15 or 20 millimeters in diameter, are seen in great profusion. The surfaces of the *intestine* are everywhere adherent. The omentum is thickened and filled with abscesses. The organs of the pelvic cavity are so bound by adhesions and contain so many abscesses that they can only be removed with a knife.

The *spleen* is enlarged, soft, and studded both on the surface and internally with small cystic abscesses similar to those found in the other organs. The pulp is exceedingly soft, dark-red in color, and there are numerous small areas of intense congestion corresponding to the Malpighian bodies.

The *pancreas* contains a number of the abscesses and is hæmorrhagic for a distance of about 5 centimeters from its splenic end.

The *liver* is enlarged, firmly adherent to all surrounding structures, very soft, friable and studded with little, grayish, hard areas, particularly along the connective tissue bands. A number of abscesses, mostly subcapsular, are found in this organ.

The *gall bladder* contains about 15 cubic centimeters of almost colorless bile and the ducts are open. Its wall is much thickened, firmly bound down by adhesion and surrounded and impregnated with abscesses. The *scrotum, epididymis* and left testicle contain a number of these small abscesses and the prostate gland is similarly involved.

The wall of the *large intestine* is very much thickened and is surrounded and infiltrated with abscesses. The *mucous* surface is free from ulceration, but shows a number of the previously described cystic abscesses just under its surface. This condition is most marked low down in the rectum and around the opening into the appendix. The appendix itself is involved in its walls and also externally, but not on its mucous surface. The entire *small intestine* shows the condition found in the large one, excepting that the changes are much more extensive and in several places in the ileum the abscesses in the wall have ruptured on the mucosa, leaving ulcers with ragged margins. The fibrous adhesive bands associated with broken-down cysts and abscesses in the mucosa of the bowel are very extensive and in some places they apparently almost obliterate the lumen of the bowel. The *stomach* is surrounded by a number of abscesses, but both its internal surface and wall are apparently free from the infection. The abdominal wall below the liver, on the right side, contains a knotty mass of abscesses several centimeters in diameter and extending well down behind the kidney.

Both *kidneys* are bound to a mass of proliferated tissue, abscesses and adhesions, and both of these organs contain a number of abscesses like the ones which have been described and which are most numerous just under the capsule.

The muscles of the calves of both legs and those of the thigh show abscesses which are from 3 to 5 millimeters in diameter.

The *cerebro-spinal canal* was not opened.

A *microscopic examination* shows parasites and eggs in the contents of many of the abscesses, but not in all. The former are found in the heart, lung, kidney, intestine, spleen and abdominal wall. Living parasites were extracted from the pectoralis major muscle and some were found free in the abdominal cavity; these were probably liberated by the rupture of some of the cysts during autopsy.

Case No. 3 (32625).—Paragonimiasis, extensive infection with P. westermanii; amœbiasis of the colon; death; autopsy.

The patient a Filipino, 50 years of age, has the following hospital record: Admitted to hospital October 21, 1905, with a diagnosis of acute beriberi; on October 23 he was transferred to the beriberi hospital; on February 23, 1906, he returned to the prison hospital with a diagnosis of chronic diarrhœa. From February 17 to 28 his temperature was 36°.5 to 36°.8, pulse 99 to 100, stools 2 to 11 in twenty-four hours. No cough was noted. From March 1 to 31 his temperature was 36°.5 to 37°.3, pulse 98 to 101, stools 6 to 13 in twenty-four hours. The diarrhœa was very persistent and not to be controlled by astringents or enemas. From April 1 to 30 his temperature was 36°.8 to 37°.2, pulse 98 to 100; the severe diarrhœa continued during the month and microscopic examination of the fæces, on April 9, showed amœbæ and red blood corpuscles. From May 1 to 31 the temperature was 36°.4 to 39°. The diarrhœa continued and there was moderate cough, which was worse at night. A urine examination

on May 3 showed nothing abnormal and a sputum examination on May 29 was negative for tubercle bacilli and for parasites or eggs. From June 1 to 30 the temperature was 36° to 39°, the lowest point usually being during the early morning hours, but on a few occasions this relation was reversed. The cough became much worse during this month and on June 6 there was a hæmorrhage of about 100 cubic centimeters from the lungs. Examinations of the blood from this hæmorrhage and of the sputum between June 21 and 29 were negative for tubercle bacilli and for parasites and eggs. On June 29 the stool still contained amœbæ and considerable blood and mucus was also noted therein. From July 1 to 4 the temperature was 36° to 37°.2. Hæmoptysis of about 500 cubic centimeters occurred again on July 3, and an examination of this specimen was again negative. Following this last hæmorrhage the patient sank slowly and he died on the morning of July 4 with a clinical diagnosis of amœbiasis and sprue.

Autopsy twelve hours after death: The body is extremely emaciated, the skin normal, the subcutaneous fat very scanty, the muscles wasted and very pale and friable. The superficial lymphatics are all enlarged. One, in the left groin, and two in the right axilla are partially broken down and contain eggs of *P. westermanii*. A small, subcutaneous abscess at the back of the neck and another in the left mammary region are noted. Both contain fluke eggs. Upon opening the chest a number of dark, slate-colored, broken-down glands are found on the under surface of the sternum; a similar condition extends throughout over the parietal pleuræ on both sides. Both *pleural cavities* are obliterated by old adhesions, and all tissues, including the lung, pleural and extra pleural structures contain abscesses from 5 millimeters to 2 or 3 centimeters in diameter. Both lungs contain numerous congested areas which on section resemble bronchopneumonia. In most of these areas numerous parasites and ova are to be found. A number of the bronchial glands are broken down and have the general appearance of the other infected tissues.

The *diaphragm* is thickened, adherent to all adjacent structures and contains numerous abscesses of various sizes.

The *pericardial cavity* contains a small amount of serous fluid and numerous adhesions are present. Both the parietal and visceral serous surfaces are covered with small, raised, dark-bluish or brownish congested spots which on section are shown to contain ova; furthermore, there are at least two adult trematodes just beneath the visceral pericardium, in the region of the right auricle. The heart muscle is very brown, but no ova are found in its substance.

The *abdominal cavity* contains large numbers of adhesions between the omentum and the other structures. In several places large areas of the omentum are puckered and brought to a central point of adhesion in the abdominal wall, and at these places parasites or eggs are invariably found. The omentum in general is thickened and contains numerous abscesses similar to those in other parts of the body.

The *spleen* is enlarged and adherent to the diaphragm and abdominal wall. It contains a number of superficial abscesses, which show both parasites and ova. On section it is rather firm, bloodless and without increase of pulp. No abscesses or parasites are found in the deeper portions of the organ.

The *liver* is of normal size, adherent to the diaphragm, abdominal wall and intestine and contains numerous subcapsular abscesses. The organ is rather firm and on section shows some increase in the interstitial tissue, from which ova are to be isolated, but no abcsess exists within the parenchyma of this viscus.

The *gall bladder* is large; it contains a considerable quantity of light-colored, fluid bile, no parasites or eggs are seen either in the gall bladder or ducts. Nothing abnormal is found in the portal vessels.

Both *kidneys* are of normal size. They are very pale and soft, with nonadherent capsules. The left kidney contains two subcapsular abscesses and one is seen in the pelvis. The adrenals appear to be normal.

The left *psoas muscle* contains an abscess with about 100 cubic centimeters of matter having the appearance of anchovy sauce, in which hundreds of parasites and eggs are encountered. There are a number of smaller abscesses in the posterior abdominal wall, on both the right and left sides.

The *prostate gland* and *epididymis* contain a few abscesses.

The *bladder* appears to be normal.

The *entire large intestine* is thickened, of a dark-slate color, and it shows a number of hard nodules beneath its peritoneal surface. On section, numerous ulcerations extending from the rectum to the cæcum are found. These ulcers vary in size from 2 millimeters to 10 millimeters. They bear no relation to the mesenteric border or to any other definite anatomic structure. Their margins are raised, appear as if they were punched out, are rather hard, granular and sometimes intensely congested; in other instances they are without congestion. The floor of these ulcers is either in the submucosa or it extends down to the muscular layer. They vary much in size, contain a dark-colored, thickened matter, together with numerous ova and in one instance a parasite.

The lower portions of the *small intestine* and *appendix* are similar to that of the large, but the upper two-thirds of the small bowel is apparently free from parasitic infection.

The *stomach* and *pancreas* appear to be normal.

A most striking general picture of this autopsy, as well as in the two preceding ones, is found in the peculiar, dull-slate color of all the tissues involved in the infection. This is particularly noticeable in the omentum, intestinal wall, and in the other tissues of the abdomen.

The abscesses referred to are of a peculiar appearance and are characteristic. They vary very much in size, but the general appearance in every instance is the same. There is a rather definite limiting cystic wall, of a dull-blue slate color, and on section a dark material like anchovy sauce is found. In most instances these abscesses contain either parasites or ova, or both.

Case No. 4 (37995).—Jacksonian epilepsy, paragonimiasis of the brain, lungs and abdominal organs; death, autopsy.

The patient, a male Filipino, 30 years of age, was admitted to the hospital with an epileptic seizure and lived about twenty-four hours, during which time the attacks were repeated two or three times. Nothing is known of the previous history of this patient except that he was in the hospital on two occasions during the present year suffering from acute coryza. During his last illness there was no fever, and the epileptic attacks were typical in every way of epilepsy major.

AUTOPSY four hours after death: Body of a well-developed, well-nourished Filipino man. Skin and mucous membranes appear normal. Two small, bleeding surfaces on the tongue, evidently from injury during his epileptic seizures. There is some œdema of the lower eyelids and a very marked, chronic conjunctivitis. The mucous membrane of the nose is also hypertrophied and œdematous. The subcutaneous tissues contain a moderate amount of fat and are normal in appearance; the subcutaneous lymphatics are not enlarged, except in the right axilla, where there is moderate hypertrophy without any evidence of an acute process.

The *muscular tissues* are rather coarse and quite pale in color. Both *pleural cavities* contain a small amount of cloudy, serous fluid and a number of chronic adhesions, these adhesions being diffuse over the visceral surface and collected in points of attachment on the parietal surface. At these points of attachment, along the ribs, are found a number of slate-colored, cystic abscesses which, on section, are typical of those already described for paragonimiasis. Both *lungs* are rather voluminous and there is a marked bronchitis of all of the larger and medium sized tubes. In the left lung there are several areas of bronchial pneumonia due to *P. westermanii*. No parasitic areas are found in the right lung.

The *visceral* and *parietal* layers of the *pericardium* are adherent in several places and, on separation of these adhesions, there are a number of raised, brownish, granular patches which contain eggs of the parasite in question. The heart muscle itself is firm and normal in color and no lesions of the endocardium are found.

The *abdominal cavity* is free from adhesions, except around the duodenum, where there is a mass of old adhesions surrounding a post-peritoneal abscess which leads well above and behind the left kidney; this contains about 50 cubic centimeters of material resembling anchovy sauce and a number of adult parasites and eggs. No direct connection between this abscess and any of the organs can be established.

The *spleen* is of normal size and consistency and no evidence of disease in it was discovered on section.

The *liver* is slightly cirrhotic and the gall bladder and bile ducts are moderately distended with fluid, which microscopically is free from any abnormal elements. No abnormal changes were found in the kidneys, bladder, or other of the pelvic or abdominal organs.

The *intestine* unfortunately was not opened.

The membranes of the *brain* are thickened and adherent in many places; bound in these adhesive masses are cystic parasitic abscesses similar to those of the pleural cavity. The choroid plexus is coarse and granular, slightly bluish, and a few eggs are found in its substance. The brain substance itself appears to be normal, with the exception of moderate congestion near the cortical surface. No distinct abscess cavity was found in this organ.

Case No. 5.—Pulmonary tuberculosis; pulmonary pleuritic, diaphragmatic, omental, intestinal and lymphatic paragonimiasis; death; autopsy.

Practically nothing is known of the clinical history of this case; the patient continued to perform his duties to within about twenty-four hours of death, at which time he first came under observation; no microscopic examinations were made during life. When admitted to the hospital he was very weak, moderately emaciated, was coughing considerably and complained of pains in his left chest and abdomen. There was an active diarrhœa and a slight elevation in temperature.

Autopsy eight hours after death: Pulmonary tuberculosis and a rather extensive infection with *P. westermanii* are found. The tuberculosis involves the bronchial glands and the upper lobes of both lungs. Some of the lesions consist of caseous areas, from 2 to 5 millimeters in diameter, and there are also several tuberculous cavities of about equal size, and one 10 millimeters in diameter is found in the apex of the left lung. Very few miliary tubercles are encountered.

The *Paragonimus* lesions of the *lungs* are very much scattered, as are the tuberculous ones, and they so closely resemble the cavities of tuberculosis that had it not been for the more extensive distribution of the *Paragonimus*

cysts in other organs, the double infection in the lungs would probably not have been discovered. Many of the tuberculous lesions show a bluish color, similar to that constantly observed in those due to Paragonimus infection and it is worthy of note that one cavity contains both tubercle bacilli and an adult *P. westermanii.*

The *Paragonimus* lesions in the *pleuræ, diaphragm* and *abdominal organs* are similar to those described in the previous cases.

Case No. 6.—Paragonimiasis of intestine, omentum, pancreas, diaphragm, abdominal lymphatics, and left pleura; chronic beriberi; death; autopsy.

The patient, a native male about 40 years of age, was admitted to hospital for chronic diarrhœa, which he stated was of long standing; he also said that he had suffered from acute beriberi about eight months before the time of his admission and that he was still suffering from this disease. Death from exhaustion and intestinal hæmorrhage occurred five days after he came under observation. On admission, the patient complained of great weakness, diarrhœa, and partial paralysis, principally involving the lower extremities. There was no cough and no pain in the chest. Emaciation was very great and anæmia pronounced. There was moderate atrophy of the lower extremities and all the reflexes were absent.

Autopsy nine hours after death: Paragonimus lesions similar to those already described under the other cases are found in the *intestinal wall,* the *peritoneum, omentum, mesenteric lymphatics, diaphragm, small intestine* and *left pleura.* No such lesions are observed in the *lungs,* although a most careful search was made, and these organs are normal, excepting a moderate congestion and œdema. The *left pleura,* particularly on its parietal layer, is moderately infected and this condition is more marked toward the base of the chest, this infection apparently being continuous with the lesions along the diaphragm. The most advanced lesions are found in the *abdominal cavity,* and particularly in the omentum, where some of the slate-blue cysts 10 to 15 millimeters in diameter are observed.

Lesions other than the specific and definite cysts due to *Paragonimus* infection are as follows: Moderate, fatty degeneration and passive congestion of the liver; slight increase in the size of the spleen with some fibrosis and perisplenitis; moderate cirrhosis of the kidneys and old, healing amœbic ulcerations of the colon.

As is true of the other cases studied, parasites or eggs are found in many, but not in all the cysts.

Case No. 7.—Intestinal, omental, and lymphatic paragonimiasis, acute dysentery and chronic parenchymatous nephritis; death; autopsy.

Practically nothing is known of the clinical history of this patient. The most interesting feature of the case is the complete absence of lung or other thoracic lesion, in the presence of a well-defined *Paragonimus* infection of some of the abdominal organs. There are two typical lesions due to *P. westermanii* on the under surface of the diaphragm, on the left side.

Case No. 8.—Paragonimiasis of the left lung, pleura and superior surface of diaphragm; acute generalized tuberculosis; death; autopsy.

The interesting features of this case are as follows: The parasitic lesions are confined to the thoracic cavity; they are associated with tuberculosis and the similarity between some of the tuberculous and the *Paragonimus* lesions is striking. The bluish color of the parasitic abscesses is less marked than in the

other cases and a similar appearance of the abscesses of tubercular origin is more decided than it is usually. Tubercle bacilli and the eggs of *P. westermanii* were found together in some of the lesions.

Cases Nos. 9 to 17.—These are all cases which have only been observed clinically, in which the diagnosis has been made by the finding of the eggs, either in the sputum or stool. These cases will not be reported in detail but the more or less careful clinical findings will be embodied in their appropriate places in this paper.

VI. ETIOLOGY.

A. CONTRIBUTING CAUSES.

The contributing causes which bring about infection with this organism, of course, can not completely be elucidated until the life cycle of the parasite has been fully worked out. However, a number of points deserve consideration.

(*a*) GEOGRAPHICAL DISTRIBUTION.—In the opinion of some of the best zoölogists, not all of the parasites which have been reported as *Paragonimus* are of the species *westermanii,* but until such time as this confusion is made more clear, it seems advisable to consider the geographical distribution of this disease as including all points from which the parasites have been reported either for man or other animals. Considered in this broad sense, the geographical distribution would include practically all of Japan, points in Korea, Formosa, China, Holland (Amsterdam), Germany (Hamburg), Sumatra and the United States, and to this list the Philippine Islands must now be added. It is almost certain that the increased interest which the importance of this subject demands will result in the finding of the infection in many places where it has hitherto been unsuspected.

(*b*) AGE, SEX, RACE, OCCUPATION, CLIMATE, AND PERSONAL HABITS.—*Age* is probably not a factor in the etiology of the disease, excepting to the extent that, as in many other infections, the exposure is greater and the infection correspondingly more frequent during the more active years of life. Stiles from the statistics up to 1900, compiled 59 cases, 45 of which were between the ages of 11 and 30 years. Four cases were in children under 10 years of age and one in an individual over 50 years old. My 17 patients ranged from 20 to 62 years of age. Eleven of them were between 25 and 35.

Sex.—The disease is much more frequent in males than in females. This has been noted by several Japanese observers and in a recent conversation with me, Professor Tokishige again emphasized this fact, at least in so far as Japan is concerned. Stiles and Hassall's statistics show 58 males out of 66 cases. My cases have all been in males, but it must be understood that in compiling this series my opportunities for observation have not been such as to allow me to judge in regard to females.

Occupation.—The majority of writers attribute very little importance to occupation as a factor in the etiology of the disease. Many of the reported cases have been among those whose vocation brought them in contact with soil and water. My cases have all been among people of the lower classes, where many of the different occupations offer similar types of exposure and where the vocation is often changed from day to day. Of 9 patients in my series where the occupation was given, 6 were fishermen, 2 were cooks and 1 a laborer. So far as I know, fishermen have not been considered especially susceptible in Japan.

Climate.—Katsurada states that the disease is more common in the mountainous region of Japan.

Physical condition and personal habits.—Some writers have considered cold and other infections to be predisposing factors, while others state that healthy persons are equally susceptible.

An examination of my cases does not indicate any especial susceptibility due to the personal habits or to the physical condition of the patient. As may be noticed from the protocols, other diseases, which probably antedated the fluke infection, were present in some instances, while in others the parasitic disease was apparently the only contributing cause of death. The association of tuberculosis, amœbiasis and other diseases with paragonimiasis will be discussed in another part of this paper.

B. SPECIFIC ETIOLOGY.

Trematodes in general.—The zoölogical position of parasitic flukes is shown in Table No. 1, and the principal diagnostic points of the parasites and ova are given in Tables Nos. 2 and 3. In addition to this, however, it seems advisable to enter somewhat more into the zoölogical details, because of the very great importance of the infections to which trematodes may give rise.

There are two classes of the *Platyhelminthes* or flat worms of interest to medical men. These are the *Cestoda,* which have no digestive tube, and the *Trematoda,* which have a more or less well-developed digestive apparatus without an anus. The order *Malacocotylea* of the class *Trematoda* contains 4 families and 10 genera or collective groups, with 15 species which interest us as medical men. There are certain more or less general characteristics of the members of the order which here may briefly be noticed, because they tend to simplify the study of the species which directly concerns us.

Nearly all parasitic flukes are hermaphroditic, with two important exceptions, namely, the two species of the genus *Schistosoma* (*S. hematobium* Bilharz and *S. japonicum* Katsurada), in both of which male and female adult parasites develop. They are all rather small, nonsegmented worms of various shapes, but for the greater part they are of an

indefinite oval form. There are one or more suckers and in a few instances one of these is armed with hooklets. The mouth or oral sucker also performs the function of the anus. The *cuticle* in most species is in part covered with scales or spines, but these are entirely absent in others. The *muscular* system is rather poorly developed, it consists of a series of fibers just beneath the cuticle and what is known as the parenchymatous muscle, which sends branches throughout the body. A *nervous* system, also poorly developed, consists chiefly of two or three ganglionic masses near the head, with their corresponding trunks and branches to various portions of the body. The *digestive* tract consists of a mouth (oral sucker), pharynx, and œsophagus, which divides into two intestinal cæca, which in turn, in a more or less winding manner, reach to the posterior portion of the parasite and terminate as blind sacs. In the genus *Schistosoma* there are one or more unions and separations of these intestinal cæca before they end in the posterior portion of the parasite The *excretory* system is primitive, but fairly well developed. It begins in excretory cells located in various parts of the body which lead by channels with the usual anastomoses, to an opening in the posterior portion of the parasite, called the excretory pore. The *reproductive* system is well developed and shows considerable variation in different species. In the main, the prominent features are about as follows: The two testicles are usually situated in the posterior portion of the worm, and are of various shapes. Each one is connected by a seminal duct with the *vas deferns,* which in turn passes forward and ends in the cirrus pouch which is on the ventral surface and closely connected with the genital pore. This pouch also contains the cirrus or penis. From the vulvar opening the vaginal tube is continuous with a well-developed uterus which usually has many folds and terminates in the shell gland at the cotype. It is indirectly continuous through the cotype with other tubes which also enter the latter as follows: The oviduct which connects directly with the ovary, the vitelline duct which is formed by tubes connecting, with the yolk glands or vitelline follicles and Laurer's canal, which is a small canal of unknown function opening on the back of the worm and often distended at its inner end into a *receptaculum seminis.* Ova pass out through the vaginal outlet and at the time of oviposition may or may not contain a ciliated embryo. In either case, under proper environment, a ciliated miracidium escapes from the egg and after a time enters an intermediate host. The parasite is again taken into an animal host from some one of these unknown intermediate ones and the adult parasite once more developes.

The entire life cycle of any of these flukes with the exception of that of *F. hepatica* Linn. is not known, but it is probable that the intermediate hosts will be found among the same class of mollusks as the ones which harbor *F. hepatica.*

TABLE No. 2.—*Showing the principal diagnostic points in the diagnosis of flukes.*

	Size.	Shape.	Color.	Oral sucker.	Ventral acetabulum.	Skin.	Pharynx.	Œsophagus.	Intestine.	Genital pore.	Male organs.	Female organs.	Habitat.	Geographic distribution.
M. lentis Gescheidt	0.00022 long.												Crystaline lens of man	Russia (Odessa), 1 reported case.
A. ophthalmobium Diesing	¼ to ½ line × ⅓ line.	Ovate-lanceolate; variable.		Orbicular, terminal to subterminal.	½ larger than oral sucker, subterminal, circular aperture.								Between crystaline lens and capsule of man.	Germany (Dresden).
O. felineus Rivolta	0.008–0.013–0.018×0.00125–0.0025	Broad flat, lanceolate, anterior end conical, posterior end rounded, partial constriction at anterior ⅓.	Reddish, transparent	0.00028 to terminal tenuis-terminal.	Size, 0.00028 at constriction between anterior ⅓ and posterior ⅔ of body.	No spines.	Small, 0.00020 long × 0.00016 broad.	0.0002 long.	Extends to posterior end of body.	Just anterior to ventral acetabulum.	Testicles lobate.	Uterus median, thick, compact ovary, slightly lobate; shell gland diffuse, composed of unicellular glands; receptaculum seminis, post lateral of ovary; vitellaria lateral in mid one-third of body and composed of 7 to 9 groups of acini on each side.	Gall ducts of cat dog glutton, and man.	Germany, Holland, Italy, France, Russia.
O. noverca Braun	0.009–0.0125 × 0.0025	Lanceolate, more attenuate anteriorly.		Size (?) terminal.	Size much smaller than oral sucker, distant about ⅓ body length from oral sucker near bifurcation of intestine.	Many spines.	Large.	Apparently absent.	Extends to posterior one-eighth of body.		Testicles apparently round or lobate in posterior ⅓ of body.	Uterus apparently poorly developed; vitellaria apparently extend from ventral acetabulum to posterior testicle.	Gall ducts of man and pariah dogs.	India.
O. sinensis Cobbold	0.010–0.020 × 0.002–0.005	Flat, lanceolate to oblong oval attenuate anteriorly, rounded posteriorly.	Reddish, nearly transparent.	Larger than ventral.	At junction of first and second fourths of body.	No spines.	0.00022 in diameter globular.	0.00017 long bifurcation nearer oral sucker.	Slender extending to posterior end of body.		In posterior one-third of body and branched.	Uterus moderately developed ovary trilobate just anterior to large, elongate vesicula seminalis; vitellaria moderately developed and occupy about middle ⅓ of body.	Gall ducts pancreatic ducts, duodenum and stomach of man and cats.	Asia sporadic imported cases elsewhere.
F. buskii Lankester	0.021–0.037 × 0.0055–0.012 or 0.014 × 0.005–0.002 thick; maximum breadth in equatorial portion.	Ventral surface flat, dorsal slightly convex, margins thin.		0.0005 in diameter, 0.0003 deep, ventro-subterminal.	0.0016–0.002 in diameter elongated caudally under ventral surface in a sack 0.002–0.008 long; center is 0.0018–0.002 from anterior end of body.	do.	Prepharynx, 0.00028; pharynx, 0.0007.	Very short; bifurcation about on anterior plane of acetabulum.	Two characteristic curves toward median line, one at equator, other between testicles.		Cirrus pouch cylindrical, median, nearly as long as body, 0.0028 to 0.0033 thick, straight contains long vesicula seminalis with a long blind sack, testicles, one posterior to other.	Vitelline reservoir, small shell gland [illegible]	Small intestine of man	Asia.
F. rathouisi Poirier	0.025–0.016	Oblong oval, obtuse, anterior end has cephalic cone 0.008 to 0.005 broad.	Whitish, tinted with brown on margins.	(?)	0.002 in diameter, 0.002 from oral sucker.	do.	(?)	(?)	(?)		Testicles side by side.	Ovary caudad of transverse vitelloduct.	Intestine or gall ducts of man.	Do.
H. heterophyes Siebold	0.001–0.0017 × 0.0003–0.0007	Elongate, oval.	Reddish.	0.00019 in diameter, terminal to subterminal.	0.00023 in diameter about the middle of the body.	Quadrate scales 0.0035–0.006 long, distal margins serrate with 8 to 9 points.	Prepharynx may reach to 0.00050. Pharynx, 0.000350–0.000070 long and 0.000040 to 0.000050 in diameter.	Extends to a point about midway between oral sucker and center of acetabulum.	Thin extend posteriorly to excretory bladder.	0.00023 in diameter.		[illegible] ventral to the [illegible] intestinal cæca.	Small intestine of man and cat and dog.	Egypt and Japan.
P. westermanni Kerb	Stiles 0.008–0.016 × 0.004–0.008; 0.002–0.005, Keilhedt, 0.01–0.020 long.	Plump, variable anterior end bluntly rounded, posterior end less blunt.	Pinkish to reddish brown.	Lenkart 0.00053–0.0075 of mole Stiles and H. 0.0008–0.00112 0.0008 0.00084 Kerbert 0.00078 to terminal to subterminal.	Lenkart 0.0006–0.0075, Kerbert 0.0078, Ward 0.0075–0.00107, Stiles and H. 0.00085–0.0022 × 0.0086–0.00144; slightly larger than oral sucker; situated 0.002–0.004 back of oral sucker.	Broad, scale like spines. Lenkart large in head dorsal body Kerbert, largest on anterior portion; Stiles and H., smallest around mouth.	Elongate.	Very short, bifurcation [illegible] acetabulum.	Somewhat zigzag to posterior end.		Often indistinct close to caudal margin of acetabulum may be in median line or to right or left of it.	Cirrus and efferent ducts straight testicles one slightly posterior to the other on either side of median line.	[illegible] and ejaculatory vas; uterus massed, opposite ovary, but may partially cover that organ; vitellaria marginal highly developed, extend from anterior to posterior extremities; Laurer's canal present.	[illegible] and occasionally man.	China, Japan, Formosa, India, Java, and United States.
F. hepatica Linn.	0.018–0.051 × 0.004–0.013 broad.	Conical anterior end on an elongate oval leaf-like body.	Pale brown to slate.	0.001 in diameter, round and terminal.	0.0016 in diameter, 0.003–0.004 behind oral sucker.	Numerous; placed side by side in alternating rows.	Elongate, 0.0007.	0.0004 broad, 1 to 1½ times as long as pharynx; bifurcation anterior to genital pore.	Dendritic; extends to caudal end of worm.	Median; halfway between oral sucker and acetabulum.	Cirrus often extended from pore; cirrus pouch, testicles profusely branched.	Vulva at side of cirrus; uterus [illegible] ovary convoluted.	Gall ducts, lung (occasionally), liver of cattle, sheep, swine, and other mammals; rare in man.	Europe and United States.
F. gigantica Cobbold	0.025–0.075 × 0.003–0.012	Flat oblong, lanceolate.		0.00112 in diameter.	Larger than oral sucker.	Present.	(?).	Extends nearly to acetabulum.	More profusely branched than in *F. hepatica*.	Median, halfway between oral sucker and acetabulum.	Testicles more profusely branched than in *hepatica*, and do not extend so far caudad.	Similar to *hepatica*, but in general more profusely branched.	Liver of giraffe, cattle, buffalo, sheep, goats; one case in lungs of man.	Africa.
D. lanceolatum Rudolphi	0.004–0.009 × 0.002–0.0025.	Thin, lanceolate.		Slightly subterminal.	Slightly larger than oral sucker, one-fifth length of body distance between two suckers.	No spines.	Small globular 0.00025.	Two or three times as long as pharynx; bifurcation just anterior to genital pore.	Extend to posterior quarter of body.	Halfway between suckers.	Cirrus pouch [illegible] genital pore to ventral acetabulum; testicles irregularly lobate, one posterior to other.	Ovary small, directly dextral posterior testicle; uterus between intestinal cæca, vitellaria moderately developed.	Gall ducts of cattle, sheep, ass, and man.	Very extended in Europe.
G. hominis L. and McC.	0.005–0.008 × 0.003–0.004.		Reddish.							Middle of anterior portion of intestine.	Two lobate testicles.		Cæcum and colon of man.	Asia.
S. hæmalobium Bilharz	Male, 0.004–0.015 × 0.001; female, 0.015–0.020.	Slender.	Whitish; female may be reddish brown.	Same size as acetabulum.	Just caudad of bifurcation of intestine.	Male, numerous small warts; female, minute spines.		Short.	Reunite caudad of testicle in the male and caudad of ovary in female.		4 to 6 glandular testicular bulbs.	Uterus rather straight, ending in bull-like ootype; ovary sacular, elongate.	Veins of man and certain monkeys.	Africa chiefly.
S. japonicum Katsurada	Male, 0.007–0.012×0.00053; female, 0.008–0.012 × 0.0004.	Slender, cylindrical.	Male, light brown yellow; female, dirty color and darker.	Terminal about 0.00029 in diameter.	A little larger than oral sucker, pedunculate.	None, except small area on anterior extremity of both sexes where there are minute spines.	Short.	Strong, muscular, 0.00029; bifurcates just anterior to acetabulum.	Unite and form terminal ampulla as in hæmatobium. Cæca may separate and reunite one or more times.	Just behind acetabulum.	Usually 6 testicles usually lobate.	[illegible] developed.	Blood and organs of man, cats.	Japan and China.

TABLE No. 1.—*Trematodes infecting man, showing the zoölogical position of flukes.*

(Order.)	(Family.)	(Genus, or collective group.)	(Species.)
Malacocotylea	Monostomidae	Monostomulum	*M. lentis* Gescheidt.
		Agamodistomum	*A. ophthalmobium* Diesing
		Opisthorchis	*O. felineus* Rivolta.
			O. noverca Braun.
			O. sinensis Cobbold.
	Fasciolidae	Fasciolopsis	*F. buskii* Lankester.
			F. rathouisi Poirier.
		Heterophyes	*H. heterophyes* Siebold.
		Paragonimus	*P. westermanii* Kerbert.
		Fasciola	*F. hepatica* Linn.
			F. gigantica Cobbold.
		Dicrocoelium	*D. lanceolatum* Rudolphi.
	Paramphistomidae	Gastrodiscus	*G. hominis* L and McC.
	Schistosomidae	Schistosoma	*S. haematobium* Bilharz.
			S. japonicum Katsurada.

P. WESTERMANII KERB.—*P. westermanii* belongs to the family *Fasciolidae* and is the type species of the genus *Paragonimus*. It was discovered by Kerbert in 1878.

(*a*) *Synonyms.*—The synonyms for this parasite as given by Stiles are in the foot note.[1]

(*b*) *General description and specific diagnosis of the parasites.*—*Size:* There are considerable variations in the measurements of the this worm as they are given by various writers. These are shown in Table No. 2. The personal equation must be considerable in trying to measure the living organism but, even after eliminating this and as much as possible all other sources of error, the differences in measurements are very large and they are often noticeable in mature specimens from different locations in the same host. The limits of variation are probably included in the following measurements: 0.008–0.020 × 0.004–0.009 × 0.002–0.006. On one occassion several parasites found in an abscess in the abdominal cavity

[1] (*a*) SYNONYMS.—*Distoma westermanii* Kerbert, 1878; *Distoma ringeri* Cobbold, 1880; *Gregarina pulmonum* Baelz, 1880; *Gregarina fusca* Baelz, 1880; *Distomum westermani* Kerbert, 1881; *Distoma pulmonis* Kiyona, Suga, and Yamagate (1881); *Distomum pulmonis* Kiyona, Suga, and Yamagate (1881); *Distoma pulmonale* Baelz, 1883; *Distoma pulmonar* La Clinica de Malaga, 1883; *Distoma pulmonum* (Baelz) Tomono Hidekata, 1883; "*Distoma hepaticum* Linn." of Miura, 1889; *Distomum ringeri* (Cobbold, 1880) von Linstow, 1889; *Distomum westermanni* Leuckart, 1889; *Distomum pulmonale* (Baelz) Leuckart, 1889; *Distomum cerebrale* Yamagiwa, 1890; *Distoma ringers* Rev. Sci., 1890; "*Mesogonimus westermanni* (Kerbert, 1878)" Railliet, 1890; *Mesogonimus pulmonalis* (Baelz, 1883) Railliet, 1890; *Mesogonimus ringeri* (Cobbold, 1880) Railliet, 1890; *Distoma westermanni* (Kerbert, 1881) Weber, 1891; "*Distoma westermanni* (Leuckart) Blanchard, 1891; "*Mesogonimus pulmonale* (Baelz, 1878)" Stossich, 1892; "*Distoma* (*Mesogonimus*) *westermani* Kerbert, 1878," of Stiles, 1894; *Distomum* sp. of Kellicott, 1894; *Distomi ringeri* (Cobbold, 1880) Simon, 1897; *Paragonimus westermanii* (Kerbert, 1878) Stiles & Hassall, 1900.

were quite large, averaging 0.015–0.018 in length, whereas those taken from the lung in the same case were only 0.010–0.015. The worms contract under the influence of all preservatives, and measurements made with specimens which have been subjected to this influence give still more uncertain results.

Color: The color, when the trematode is first removed from the animal host, varies from a dark reddish-brown to a light slate. After it has been exposed to the air for a short time, the surface takes on a dull-grayish appearance, similar to that seen in the preserved specimens.

Shape: When the parasite is alive its shape is somewhat variable, but on the whole it is fairly constant; it is oval, the more acute pole being the caudal extremity. The ventral surface is more flattened than the dorsal one and at times it is even concave, except at the extreme cephalic end, where the more spherical shape is maintained. Specimens are always altered while in preparation; this is probably due to the more rapid absorption of the chemicals by certain portions of the body and the consequent uneven contraction.

Motility: There does not appear to be much in the literature concerning the motility of these worms. The parasites do not appear to have more than a slight power of active locomotion when they are removed from the host, but motions of different portions of the body may be seen. The most interesting of these gives the trematode the ability to protrude and retract its head by stretching or contracting that part of the body cephalad of the acetabulum, and again it has the power of altering the plane of the oral sucker in a like manner, so that at times the latter may appear to be directly terminal and again almost completely subterminal. These two motions may be observed in a much more striking degree in members of the genus *Opisthorchis.*

Cuticle: A rather thick, dense skin envelopes the entire parasite, but when it is carefully studied in serial sections cut longitudinally and transversely (see Plates V, VI, VII, and VIII) it is seen that this cuticle is not of equal thickness throughout, it being heavier on the dorsal and lateral surfaces than it is on the ventral one. Even in some places on the dorsum it is thicker than it is in others. At the cephalic end, the structure of the cuticle is more closely interwoven with that of the deeper tissues.

Spines: Almost the entire body of this worm is covered with scale-like spines, which are of different sizes in different locations, and in certain places, such as the ventral surface from the acetabulum to the oral sucker, they are almost entirely absent. The spines in this situation, wherever they occur, are smaller than the others; they gradually increase in size on the lateral borders and they reach a maximum on the dorsum. This seems to be true whatever transverse plane of the body is studied, but it is particularly marked about the region of the acetabulum. Again, in

longitudinal sections, it is observed that the spines at the extreme cephalic extremity are smaller and that they become larger toward the equatorial portion and again slightly smaller at the caudal extremity. In places, such as on the dorsum, these spines seem to extend above the surface more than they do in other situations, whereas along the caudal portion of the ventral surface their projection above the surface is hardly noticeable in sections. The varying direction of these spines as they are seen in sections from different worms would suggest that, during life, the animals may have the power of moving them and, perhaps, of using them in locomotion or in holding themselves in position for other purposes. This hypothesis of motion is further born out by the unique arrangement and setting of the spines in the skin. They rise from the inner surface of this organ, penetrate it at fairly constant and parallel angles, and are very closely held in place. Alternate layers arise from a slightly more superficial layer of the skin, but these pass out, as do those from the deeper tissues.

Oral sucker: This is spherical or slightly oval in shape, the largest diameter always being ventro-dorsal, it is terminal to subterminal, and in the living parasite it may change from one to the other of these positions. Measurements have only been possible in preserved specimens, and here accurate work with a Zeiss photomicrographic apparatus gives 0.86 millimeter as an average of 10 specimens, the smallest being 0.63 and the largest 0.97 millimeter. The sucker is composed of outer and inner, rather definite, membranes which are connected by radiating fibers interspersed with small, granular cells. The outer membrane apparently connects directly with the parenchymatous muscle fibers of the parasite. The lateral lips of the sucker are heavier than the ventral and dorsal ones.

Ventral acetabulum: This is slightly larger than the oral sucker. The average measurements in the parasites used in measuring the oral sucker gave 0.92 millimeter, the smallest being 0.76 and the largest 1.31. It is slightly oval or spherical in shape, and in structure it closely resembles the oral sucker. It is situated in the cephalic half of the body, on the ventral surface. At times its surface seems to be parallel with the ventral surface of the parasite and again it appears to form quite an angle with the latter. The distance of the acetabulum from the oral sucker is a changing one during the life of the parasite; this is due to contractions and protrusions of the cephalic portion of the worm.

Pharynx: This is a constricted portion of the oro-œsophageal tube and it does not differ in structure from the œsophagus.

Œsophagus: This organ is short and finally divides into the two intestinal cæca. Together with the pharynx, it arches somewhat dorsally from the oral sucker to its bifurcation; in structure it resembles the oral sucker.

Intestinal cæca: These, two in number, rise from the bifurcation of the œsophagus and run out in a zig-zag course on either side, very nearly to the caudal end of the parasite. Sections through these organs show what appears to be a primitive mucous membrane consisting of a basement membrane with superimposed cells

Genital pore: This is small and often indistinct. In 3 out of 5 specimens it was to the left of the median line, close to the ventral acetabulum.

Male organs: These are not very well developed; the testicles lie one on each side of the median line, the one slightly more caudad than the other, and both just posterior to the uterus, however; the latter organ sometimes so overlaps one of the testicles as to render its detection difficult. The cirrus and cirrus pouch are absent.

Female organs: The rather short, compact, closely coiled uterus may lie on either side of the median line just caudad of the ventral acetabulum. The ovary is distinct, branched, and usually almost opposite and slightly posterior to the uterus.

Excretory pore: This is prominent and situated at the caudal extremity.

Vitellaria: These are numerous and well developed, covering almost the entire parasite. Laurer's canal is present.

TABLE No. 3.—*Showing the principal diagnostic points of fluke eggs.*

	Size.	Shape.	Color.	Operculum.
M. lentis Gescheidt				
A. ophthalmobium Diesing.				
O. felineus Rivolta	Styles, 26–30 × 11–15	Oval	(?)	Well defined on the more acute pole.
O. noverca Braun	34 × 19–21	do		(?)
O. sinensis Cobbold	27–30 × 15–17	do	Dark brown	Sharply defined.
F. buskii Lankester	120–130 × 77–80			
F. rathhouisi Poirier	150 × 80	Ovoid		
H. heterophyes Siebold.	20–30 × 15–17	Oval	Light brown	(?)
P. westermanii Kerbert.	Leuckart, 80–100 × 56; Ward, 96–118 × 48–53; Stiles and Hassall, 68–96 × 48–60.	do	Yellow shell	Present.
F. hepatica Linn	130–145 × 70–90	do		
F. gigantica Cobbold	150–190 × 75–90			
D. lanceolatum Rudolphi.	38–45 × 22–30			
G. hominis Lewis and McConnell.	150 × 72	Oval		Do.
S. hæmatobium Bilharz.	135–160 × 55–66	do		Not present; usually terminal or subterminal spine.
S. japonicum Katsurada.	58–90 × 30–72.5; Woolley, 62.4–72.8 × 43.6–48.	do	Yellow brown.	No spine or operculum.

TABLE No. 3.—*Showing the principal diagnostic points of fluke eggs*—Continued.

	Miricidum.	Sporocyst.	Redia.	Cercaria.	Intermediate host.
M. lentis Gescheidt	------	------	------	------	
A. ophthalmobium Diesing.	------	------	------	------	
O. felineus Rivolta	Contains ciliated embryo at oviposition.	Not known	Not known	Not known	Unknown.
O. noverca Braun	(?) Unknown	do	do	do	Do.
O. sinensis Cobbold	Contains ciliated embryo at oviposition.	do	do	do	Do.
F. buskii Lankester	------	do	do	do	Do.
F. rathhouisi Poirier	------	do	do	do	Do.
H. heterophyes Siebold.	Thick shell; contains ciliated embryo at oviposition.	do	do	do	Do.
P. westermanii Kerbert.	Ciliated; developes after egg leaves the host.	do	do	do	Do.
F. hepatica Linn	Conical, ciliated, with one papilla, two cup-shaped eye spots and rudimentary intestine.	Found in small snails of genus *Limnæ*.		Whitish and found encysted on plants.	Snails.
F. gigantica Cobbold	------	------	------	------	
D. lanceolatum Rudolphi.	Contains embryo when oviposited.	------	------	------	
G. hominis Lewis and McConnell.	------	------	------	------	
S. haematobium Bilharz.	Develops after oviposition.	------	------	------	
S. japonicum Katsurada.	Elongate, oval, ciliated on anterior portion.	------	------	------	

Ova: The eggs are oval in shape and vary in color from a reddish-brown to light-yellow, the color depending somewhat upon the stage of their development and the source from which they are obtained and perhaps, also, upon other conditions which are not fully understood. Again, their size varies considerably, and a glance at Table No. 3 will show the marked differences in the measurement given by some of the principal observers. I have carefully measured several specimens with the Zeiss photomicrographic apparatus with the following results:

Length, 0.0062 to 0.0098; average, 0.0074.
Breadth, 0.0047 to 0.0063; average, 0.0057.

Eggs in sections of tissues and those preserved in any other manner contract somewhat and these are not considered in the measurements given above. A well-marked operculum is probably present in all

mature specimens, but in many instances this is indistinct and at times it can not be made out at all. This operculum has quite a distinctive appearance which is noticeably different from that of some of the other fluke eggs. The operculum in the ova under consideration appears to fit into an opening very much in the manner of a cork into a bottle, whereas in some of the other trematodes, particularly *Opisthorchis,* the opercula appear to be placed over openings more in the fashion of a cap.

The *ovic cell* in many specimens is quite distinct, and several *yolk cells* are then also present, but in others, even if they are taken from the same abscess, no such structure can be made out.

(*c*) *Life cycle.*—The life cycle of this worm is unknown; this fact is brought out by Table No. 3. When the eggs are oviposited they do not contain an embryo, but Manson and a few other observers have succeeded in hatching free swimming, ciliated miracidia from these eggs by placing them in water for given lengths of time. I have repeated these experiments many times, but so far have not succeeded in obtaining the miracidia. The sporocyst, redia, cercaria and intermediate host or hosts are absolutely unknown, but reasoning from analogy it is probable that the intermediate host will be found to be some form of edible snail.

(*d*) *Habitat.*—The habitat is in man (all tissues and organs) the dog, cat, hog, cow and tiger. In the Philippine Islands it has been found in man and the cat. The men under my observation were one Chinaman and two Japanese, the others being native Filipinos. Thirty-two autopsies on cats were performed and although fluke infections were present in over 60 per cent of the animals, *P. westermanii* was found but once. It has not been encountered, even after careful search in rats, dogs, or monkeys.

(*e*) *Distribution in the body.*—The parasites or eggs have been reported according to previous literature in the following places: The lung, brain, eyelids, liver, intestinal wall, omentum, diaphragm, cervical glands, in Poupart's ligament, the perineum, appendix, rectum, peritoneum, cirrhotic liver, and free in the abdominal cavity.

Looss and other careful workers doubt the diagnosis in some of these cases. However that may be, I now wish to confirm every one of the above-mentioned sites of infection and to add to them practically every other tissue and organ in the body. Particular attention may be called to the spleen, skin (ulcers), lymphatics, pancreas, heart and pericardium, the epididymis, urinary bladder, psoas and other muscles, and many other places. In fact, in some of my cases which have been described above the distribution of the parasites, eggs and lesions was sufficiently universal to justify the term of *general infection.*

(*f*) *Primary points of infection and manner of spread in the body.*—The exact mode of infection can not, of course, be determined until the

life cycle of the parasite is further elucidated. Considering the facts which are available, it has generally been supposed that the infection is taken into the gastro-intestinal canal through food or drink. However, it has been difficult to reconcile this conclusion with the next, quite generally accepted, statement that the lungs are the primary seat of lesions and, indeed, are the only organs involved in many of the cases. Several observers believe that the worms reach the lungs by wandering from the œsophagus into the trachea and then through the bronchial tubes. Katsurada considered that the young worms could bore through the intestinal wall and reach the lungs by the lymphatics and Yamagiwa thought that they could enter them by penetrating directly through organs and tissues. All have agreed that the brain lesions which are often encountered are secondary to the pulmonary ones, and that the infection reached this organ through the blood vessels.

Considering our present knowledge of the subject, infection through the gastro-intestinal canal must be accepted but the possibility of infection through the sound or broken skin can not be excluded. Furthermore, from the facts brought out in this report, the lungs can not be considered as the primary seat of lesions nor even in many cases as the most important organs involved.

The observations made in Manila further convince me that the spread of the infection, when it is once established, is chiefly by the lymphatics, as was originally pointed out by Katsurada. Many facts tend to support these statements. In the first place, in at least one of my cases the lungs were not at all involved and in one instance, they were the only organs infected. All the findings are compatible with the theory of gastro-intestinal infection, spread by lymphatics. Even the lung lesions often bear out this view, for, as we shall presently see, the majority of the lesions are not of the bronchiectatic type as it is generally considered, but they bear a closer relation to the lymphatic system.

VII. PATHOLOGY.

The articles dealing with the pathology of this infection prior to 1899 have been well summarized by Stiles and Hassall; the most important ones since that time have been those of Katsurada, Scheube and of Looss. Taken together, these discussions hardly present an adequate picture of the pathology of the disease as it has been seen in Manila.

In general in my cases, the distribution and severity of the lesions have been greater than is usually recognized to be the case by other writers, and the lung lesions are not as predominant as they have been accredited with being in other localities where the disease is endemic.

A. MATERIAL.

The character and the amount of material for this report has already been extensively reviewed in Chapter V.

B. METHODS.

Museum specimens have been prepared by the Kaiserling method and a fairly complete collection of specimens deposited in the Museum of the Biological Laboratory of the Bureau of Science in Manila. Another smaller selection has been forwarded to the Army Medical Museum in Washington, and still others furnished the Naval School of Tropical Medicine in Washington and other interested persons. Tissues for histologic study were fixed in Zenker's solution and in alcohol and ultimately imbedded in paraffin.

A large variety of stains has been used, including Van Gieson's, Heidenhain's iron and other hematoxylins, Borrel's and the safranin stains. Many stains are satisfactory for the reason that fine differentiation is hardly necessary for the study in sections of the organisms or eggs. On the whole, the Van Gieson has proved the most useful stain, and it is by far the most satisfactory for the study of the cuticle and spines of the parasites. Eosin and methylene-blue give a sharp and clear picture, particularly of the eggs, although these, as well as the parasites, are easily recognized even in unstained sections.

TABLE No. 4.—*Showing pathologic summary*

	I.	II.	III.
External findings	Emaciation and anæmia, marked chronic conjunctivitis. Bluish ulcer right axilla containing ova *P. westermanii.*	General nutrition good; moderate jaundice; macular skin eruption.	Emaciation extreme. Small, subcutaneous abscesses at back of neck and left mammary region and in left groin containing ova.
Lymphatics	Necrotic in right axilla and contain ova *P. westermanii.* Superficial, all moderately enlarged. Inguinal and femoral, markedly enlarged. Abdominal enlarged, some necrotic and contain eggs of *P. westermanii.*	Axillary moderately enlarged and congested.	Superficial, all enlarged, one in left groin and two in right axilla broken down and contain ova. Bronchial glands bluish and contain abscesses.
Muscles	Soft, pale and coarse. Adult *P. westermanii* in left pectoralis major and another in cyst cavity in abdominal wall.	Soft and pale. Both pectoralis major muscles contained cystic abscesses with adult *P. westermanii.* A chain of abscesses in abdominal wall on right side extending down behind the kidney. A few small abscesses in the calf muscles of both legs.	Wasted. Large left psoas abscess containing over 50 adult parasites; other small abscesses in posterior abdominal wall on both sides.
Thoracic cavity.	Many adhesions. Bluish *P. westermanii* cyst on under surface of sternum.	A few small, bluish, cystic abscesses on under surface of sternum.	Dark, slate-colored cystic abscesses on under surface of sternum.
Pleuræ	Considerable fluid with flocculi and stringy material in both. Many adhesions, both visceral and parietal, contain many bluish *P. westermanii* cysts with eggs. Some are in chest wall outside pleura.	Both cavities contain yellow, flocculent fluid with long shreds of necrotic tissue. Both visceral and parietal pleuræ and even external to the pleuræ are very numerous, bluish cystic abscesses containing ova or parasites.	Extensive obliterative pleuritis. All tissues and even extra pleural structures infiltrated with typical abscesses.
Lungs	Moderate bronchitis. No bronchiectatic cavities and no eggs or parasites free in bronchi. Numerous areas of bronchopneumonia, largest near surface. Many of these areas contain cysts with *P. westermanii*, and others contain ova. Many bluish cysts with eggs or parasites not in the pneumonia areas.	Moderate bronchitis with ova but no parasites free in the tubes. Both organs contain many areas of broncho-pneumonia, the largest one being superficial. Some of these areas appear as those of ordinary pneumonia while others surround cystic abscesses. There are also numerous bluish cystic abscesses, more numerous subpleural, which are not surrounded by pneumonic areas.	Extensively involved; areas of bronchopneumonia and abscess formation as in Cases I and II.
Pericardium	Small amount of cloudy fluid but no eggs. Serous surfaces dull and adherent over right auricle. Eggs and parasites in adhesions in brownish patches.	Normal amount of clear fluid, a few adhesions between the epi- and pericardium. Both membranes show small, brownish areas containing ova. Several bluish cystic abscesses on outer surface of parietal membrane.	Extensive obliterative pericarditis. Both parietal and visceral surfaces covered with dark, brownish, raised areas containing ova. Two adult parasites under visceral pericardium. (See Pl. I.)
Heart	Muscle brown and coarse; *Paragonimus* lesions extend a short distance from pericardium.	Surface shows many little brownish raised areas which contain ova and follow the vessels in distribution. Muscle pale and friable.	Muscle very brown. For surface see above and Plate I.

in eight fatal cases of paragonimus infection.

IV.	V.	VI.	VII.	VIII.
Well developed and nourished. Some œdema of eyelids and marked chronic conjunctivitis. Mucosa of nose hypertrophied.	Moderate emaciation.	Extreme emaciation and anæmia.	----------	----------
Superficial, normal except in right axilla where there was moderate congestion.	Not involved except in the abdominal cavity.	Superficial, normal; mesenteric and other abdominal enlarged and may contain *Paragonimus* abscesses and eggs.	Moderate *Paragonimus* infection of the abdominal lymphatics.	----------
Appear normal ----------	Pale and soft ---	Pale and wasted.	----------	----------
----------	----------	----------	Absolutely free from *Paragonimus* lesions.	----------
Moderate obliterative; pleuritis. Moderate number of the *Paragonimus* abscesses in left side and a few in the right	Very extensive *Paragonimus* infection similar to Case I.	Right normal, left contains a few *Paragonimus* abscesses and adhesions.	Appear normal	*Paragonimus* lesions of left side.
Marked bronchitis of the larger tubes but no eggs or parasites. A few pneumonic areas in the left lung and a few bluish abscesses. The right lung apparently free from the fluke infection except in areas immediately beneath the pleura.	Extensive double infection of tuberculosis and *Paragonimus*. One abscess contains both tubercle bacilli and adult *Paragonimus*.	Moderate congestion but no *Paragonimus* lesions or eggs found after a most careful search.	Appear normal	*Paragonimus* lesions of left. Tuberculosis both lungs.
Adhesions in several places which, when separated, have brownish areas containing ova.	Not involved ---	Appears normal.	Appears normal.	----------
Appears normal ----------	Not involved ---	Appears normal.	Appears normal.	----------

TABLE No. 4.—*Showing pathologic summary in*

	I.	II.	III.
Abdominal cavity.	All tissues matted together and numerous bluish *Paragonimus* cysts everywhere. These are most numerous at various points of adhesions, as between omentum and intestine or abdominal wall.	A mass of adhesions and dark, bluish cystic abscesses from 0.001 to 0.020 in diameter. Omentum thickened and simply studded with *Paragonimus* lesions. The pelvic cavity so massed with adhesions and abscesses that contents can only be removed with the knife.	Similar to Cases I and II.
Diaphragm	On the left side much thickened and adherent above and below; contains many *Paragonimus* lesions on both surfaces.	Very much thickened and contains abscesses on the left side. Both surfaces studded with small, bluish cystic abscesses.	Similar to Case II.
Spleen	Some perisplenitis with *Paragonimus* lesions at points of adhesion. Moderate increase of soft splenic pulp.	Enlarged and soft, contains both on the surface and in the parenchyma many bluish cystic abscesses containing ova.	Marked perisplenitis; organ hard and bloodless. Numerous subcapsular abscesses; deeper structure free from lesions.
Liver	Adherent to abdominal wall, diaphragm, intestine and omentum. Bluish *Paragonimus* lesions at points of adhesion. Multiple abscesses very small, many of which contain both amœbæ and *Paragonimus* eggs. Nothing abnormal in gall bladder or ducts.	Enlarged and rather soft, marked perihepatitis. Glisson's capsule increased and contains a *few* small abscesses. Numerous subcapsular abscesses. Gall bladder wall thickened and pale, surrounded and infiltrated with abscesses and one parasite found in common duct.	Chronic perihepatitis. Some increase of connective tissue with ova in places but no abscesses in deeper portions of organ. Numerous subcapsular abscesses containing eggs. Gall bladder and ducts appear normal and are free from parasites or eggs.
Pancreas	A few small, bluish cystic abscesses near the head, mostly peripancreatic, but some invading the parenchyma of the organ.	Contains a number of small abscesses and is hemorragic for 0.05 on its splenic end.	Appears normal.
Appendix	Bound in a mass of adhesions with several typical lesions involving the mesoappendix, walls and mucous membrane of the organ.	Walls and mesoappendix contain abscesses but mucosa intact except around the opening in the cæcum where there are several abscesses.	Walls and mesoappendix contain nodules and abscesses and mucosa ulcerated with ova in the scrapings.
Stomach	Not involved except in adhesions on the serous surface.	Not involved except by adhesions on the serous surface.	Appears normal.
Small intestine.	Severely involved in its entire length. Typical cystic abscesses invading all its coats and ulceration of the mucosa.	Involved throughout. The walls contain many abscesses some of which protrude into the lumen of the bowel and others have broken down leaving ragged ulcers of the mucosa. There are a number of adhesive bands partly occluding the lumen.	Upper two-thirds appears normal; lower one-third similar to large intestine.
Large intestine.	In general very similar to small intestine and in addition shows amœbic ulceration of the mucosa throughout.	Walls much thickened and contain many cystic abscesses, some of which protrude into the lumen of the bowel. There is no ulceration of the mucosa.	Walls thickened and hard, dull, slate color, and contain many hard nodules and a few cystic abscesses. Mucosa ulcerated throughout. The ulcers are punched out and surrounded by zones of congestion. The contents dark in color and contain ova. In one an adult parasite was found.

eight fatal cases of paragonimus infection—Continued.

IV.	V.	VI.	VII.	VIII.
Free from adhesions except around the duodenum where there is a mass of old adhesions covering a post-peritonial *Paragonimus* abscess leading down behind the left kidney.	Extensive *Paragonimus* infection similar to Case II.	Adhesions and ratherextensive *Paragonimus* infection of omentum and mesentery.	Moderate number of adhesions with rather extensive *Paragonimus* lesions particularly in omentum.	Tuberculosis. No *Paragonimus* lesions found.
Moderate thickening of the left side and a few cystic abscesses on the surfaces.	Extensive *Paragonimus* infection similar to Case II.	Moderate number of abscesses on left side on both upper and lower surfaces.	Two bluish cystic abscesses on under surface left side.	*Paragonimus* lesions left upper surface.
Appears normal	Not involved	Appears normal.	Slightly enlarged and soft.	Tuberculosis.
Moderately cirrhotic. Gall bladder and ducts appear normal.	Moderately firm and few subcapsular cystic abscesses.	Moderate fatty degeneration. No *Paragonimus* lesions.		
Appears normal	Appears normal.	Appears normal.		
Appears normal	Similar to Case III.	Appears normal.	Appears normal.	
Appears normal	Appears normal.	Appears normal.	Acute catarrh	Tuberculosis.
Appears normal except duodenum which is bound down with adhesions.	Severe *Paragonimus* infection of lower one half.	In lower portion a small area of bluish cystic abscesses in wall.	*Paragonimus* infection throughout. Acute dysenteric lesions in lower ¼.	
Appears normal externally	Rather extensive infection similar to Case II.	Healing amœbic ulceration.	*Paragonimus* infection throughout, lesions of acute dysentery throughout.	Tuberculosis.

TABLE No. 4.—*Showing pathological summary in*

	I.	II.	III.
Kidneys	Both organs large, soft and œdematous. Adhesions and *Paragonimus* lesions around the kidneys. Lesions under the capsule and in pelvis and ureters. Adrenals appear normal.	Numerous adhesions and subcapsular abscesses. Adrenals seem normal.	Pale and soft; two small subcapsular abscesses and one pelvic abscess in left kidney. Adrenals seem normal.
Bladder	Walls contain several cystic abscesses.	Wall thickened and contains several abscesses, some extending into the lumen of the organ. The mucosa intact.	Appears normal
Scrotum	Epididymis is swollen and contains typical lesions which extend through the inguinal canal to lymphatics in abdominal cavity.	Epididymis contains several small abscesses.	Epididymis contains a few small abscesses.
Prostate gland.	Enlarged and on section contains several cystic abscesses.	Contains a few small, bluish, cystic abscesses.	Contains a few small abscesses.
Cerebro spinal canal.	Not opened	Not opened	Not opened
Miscellaneous.	Ova or parasites found in most of the lesions mentioned but in some otherwise typical ones neither eggs nor worms were found. Amœbæ found in intestinal ulcers, liver, abscesses, in the prostate and in some of the lymphatic abscesses in the abdomen.	Ova and parasites in most of the lesions examined but not in all. This was apparently an acute case and no etiologic agent except *P. westermanii* was found. Death apparently entirely due to the fluke infection.	Many ova found extensively distributed. One psoas abscess contained more than 100 adult parasites.

eight fatal cases of paragonimus infection—Continued.

IV.	V.	VI.	VII.	VIII.
Appear normal	Appear normal	Moderate cirrhosis.	Cloudy	
Appears normal	Appears normal.	Appears normal.		
Appears normal	Appears normal.	Appears normal.		
Appears normal	One small cystic bluish abscess.	Appears normal.		
Membranes of brain thickened and adherent in many places and have many cystic abscesses, containing ova in the masses of adhesions. Choroid plexus coarse and granular, slightly bluish and contains ova. No abscesses in the brain substance.	Nothing abnormal found.	Not opened		
The post-peritoneal abscess was evidently the oldest lesion in this case.	The double infection of tuberculosis and *P. westermanii* is the notable feature of this case.	The interesting feature of this case was the freedom from infection of the lungs.	The interesting point of this case is the complete absence of involvement of the chest organs by the *Paragonimus* infection.	Combined tuberculosis and paragonimiasis. The fluke infection confined to the chest organs.

C. GROSS LESIONS.

Rather liberal abstracts from the autopsy protocols in my eight fatal cases are given in Chapter V of this report, and these findings are epitomized in Table No. 4.

All the previously described lesions, as may be seen from a study of these cases and of the literature on the subject, are found in these eight and in addition new distributions and pathological processes caused by the parasite are recorded. In three of these cases the distribution is extensive enough to justify the term general infection; in two it is so markedly predominant in the lungs that *thoracic* or *pulmonary paragonimiasis* would seem a proper designation in these instances; in one case of epilepsy the term *cerebral paragonimiasis* would more clearly indicate the nature and most active location of the processes. Whatever the location or distribution of the lessions, there is always a great similarity between them.

These *Paragonimus* lessions have certain characteristics in general, which are sufficient to make it possible usually to identify the mature ones even without finding the parasites or without using the microscope. These characteristics are the color, general structure, contents and the absence of evidence of active inflammation.

The color of the lesions is a peculiar dull, bluish-slate, without evidence of pigmentation, and it seems to be in part due to reflection from the contents through the walls of the cyst, but this is not entirely the case for, after opening and cleaning a lesion, some of this color remains in the wall.

The general structure of the mature lesion is that of a necrotic abscess with a definite and more or less dense wall, which appears to be made up of layers. The outer surface is intimately connected with the surrounding tissues and the inner one is usually a smooth appearing membrane, but it may give evidence of being granular.

The contents vary but little. In addition to adult parasites, and eggs which may or may not be present, there is a material resembling anchovy sauce filling the entire cavity. At times (probably in mixed infections) the contents may appear more like ordinary pus and again it may be caseous and hardly distinguishable from a tuberculous lesion. It must be remembered that such a double infection may be present. As a rule there is an almost complete absence of the usual evidences of inflammation in or around these lesions.

While lesions answering to the description given above are characteristic, and while some of them may be found in every case of the disease, there are several important exceptions. These exceptions are so prom-

inent that for convenience in discussion I will somewhat arbitrarily give the following classification:

(*a*) The non-suppurating lesion.
(*b*) The tubercle-like lesion.
(*c*) The suppurating (abscess) lesion.
(*d*) Ulcerative lesion.
Skin.
Mucosa.
Bronchial.
Intestinal.

(*a*) The *non-suppurating lesion* may or may not be an early one. It has three subtypes.

1. Those found on serous surfaces such as the pleuræ and, less frequently, the pericardium or meninges. These lesions are nearly always located at some point of adhesion between serous surfaces and consist in raised, brownish-colored, slightly roughened areas, which are moderately firm and which often contain ova. (See Pl. I.)

2. Those found in the loose connective tissue, for example in the subserous tissues of the intestine, and less frequently in the lung, liver and elsewhere. They consist in a simple infiltration of the tissue with eggs, without to any extent alterating the normal histological picture (see Pl. IX, fig. 1); sometimes there is seem moderate inflammatory reaction and in more advanced ones some increase in connective-tissue formation. These lesions are almost certainly early ones and immediately precede the ones about to be described.

3. Those which consist in a simple hyperplasia of connective tissue, containing ova. They are sometimes located in the cirrhotic liver and more often in the submucous and subserous coats of the intestine, and in the lung.

4. The pneumonic areas often encountered in the lung. These pneumonic areas closely resemble similar lesions from other causes and may or may not contain parasites or ova. They probably, at least in part, follow lesions of types 2 and 3.

b. Tubercule-like lesions most often are found in the lung, but occasionally are also observed in other organs.

Miura and other observers described such lesions as closely resembling miliary tubercles, but I have not found such exceedingly small and definite ones of this type. However, in the lungs and elsewhere caseating nodules are encountered which are from 2 to 10 millimeters in diameter and which are almost or quite indistinguishable from similar ones of tuberculous etiology.

c. The suppurating lesions.—These are of two kinds, the first showing early formation of abscesses, which in appearance resemble ordinary

pyogenic ones, probably followed at times by the second kind which is characterized by the development of a cyst wall. However, this is not the universal course of these lesions, for sometimes, particularly in the prostate gland and in the lymphatic glands, the ordinary type of abscess formation is more nearly maintained during the course of the infection and the cyst wall, with the bluish coloration, does not develop. Again, we find the more cystic type of development shown in some of the smallest and earliest lesions. While the ordinary lesions which appear like abscesses often contain ova, their presence can hardly be said to be characteristic of the disease, and this type of lesion is probably due, in part at least, to other etiologic influences. The bluish-slate colored, cystic, abscess-like lesions are more or less frequent in every case. They are characteristic of the disease and have already been described.

d. Ulcerative lesions are found both in the skin and mucous membranes. In both cases they are the result of perforation of lesions from the lymphatics and other underlying structures and are probably never the result of direct infection of the skin or mucosa. They are somewhat distinctive, of a slow chronic type without much acute inflammatory reaction. Their edges are often of a bluish color, and are overhanging. Their contents is of a granular nature and the opening leads to the underlying tissues. The skin ulcers most often are found in regions rich in superficial lymphatics such as the groin or axilla, and the ulcers generally communicate with infected and broken down glands. In one of my cases, two ulcers in the groin had been diagnosed and treated as "tropical ulcer." Microscopic examination of the contents of the lesions at autopsy showed the eggs of the fluke under discussion.

The ulcers of the mucous membrane are most often seen in the bronchi and in the intestine, less frequently in the bile ducts. When they are in the bronchial tubes they usually communicate with bronchiectatic abscesses and the primary lesion is in the deeper structures, as has already been described.

In the intestine, also, the primary lesion is in the deeper layers, and the breaking down of the mucous membrane with ulcer formation is a secondary result. I have not often been able to find eggs in the mucosa, but the deeper structures concerned in the ulcer may have many eggs and sometimes adult parasites. This is in marked contrast to the *Schistosoma* infection, where, for example, the mucous membrane suffers most actively and the eggs are numerous in this part of the bowel.

The intestinal ulcers are usually of irregular shape and do not bear a definite relation to the mesenteric border or other anatomical structures of the bowel. In well-advanced cases they may quite closely resemble tuberculous or amœbic ulceration, particularly when bismuth salts have been administered in the latter cases and the edges of the ulcers have been darkened by impregnation with these chemicals; this

I have pointed out in previous papers in respect to tuberculosis and amœbic dysentery.

Course and termination of the lesion.—The several types of departure from the earliest point of infection have been described, and all of these may be found in a case of extensive infection at the same time. The secondarily infected, or mixed lesions, and the process of healing which is sometimes seen may also be considered here.

Mixed lesions.—These probably occur quite frequently and they may be of several kinds. In one of my cases many of the abscesses in the liver and other organs contain amœbæ and *Paragonimus* and in two others the intestinal lesions were of this double infection. In addition to this, bacteria have been found, and while this subject has not been sufficiently investigated, it is probable that this type of mixed infection is of great importance. In case 2, which apparently pursued a very rapid course, numerous bacteria were found in the *Paragonimus* lesions and in one other the abscesses of the prostate were more of a pyæmic nature than they were of a parasitic type, although the trematodes and the bacteria were present. It would seem that what at first appeared to be a single infection and which seemed to establish for the parasites the capability of inaugurating an acute process, probably constituted in reality a double one, and that the evidences of the more acute inflammatory changes were due to the bacteria present.

Healing to the extent of complete disappearance of all evidence of the former infection probably does not take place, but by encapsulation and other connective-tissue hyperplasia the lesions may become inactive so as to produce no further disturbance. I have several times seen areas of old, bluish scar tissue which, from the amount of contraction present, probably resulted from what formerly constituted rather extensive, *Paragonimus* lesions.

D. SPECIAL GROSS PATHOLOGY.

It seems advisable at this point, after discussing the general pathological anatomy and the lesions of this infection, to introduce a brief explanatory résumé of the pathological findings which are shown in Table No. 4.

The *conjunctivitis* noted in 2 of the 8 cases was probably not due to the fluke infection. In one of these, a careful microscopic examination was not made and in the other such examination did not show ova. Similar types of severe conjunctivitis, largely of the Koch-Weeks variety, are of very frequent occurrence among the prisoners from which much this material was obtained.

Skin lesions, consisting of ulceration, were present in 2 out of 6 of the fatal cases. These ulcers in each instance communicated with diseased lymphatics and their characteristics have already been given.

Lymphatics.—Both the subcutaneous and deeper lymphatic glands suffered in at least 5 out of 7 of the 8 fatal cases. Their involvement is much more extensive and important than is indicated in the literature of the subject. In

one case (Pl. 2, fig. 2) an adult parasite was found in an abdominal gland. All types of lesions are observed in the glands and in some, where there are no distinctive abnormal features, ova may occasionally be found. The lymphatic disturbance is usually so extensive as strongly to point to the lymphatic system as the distributing agent of the disease in the body.

Muscles.—Adult *P. westermanii* were found in the pectoralis major muscles in 2 of the 8 cases and in 3 the psoas or other muscles contained abscesses.

Pleuræ.—The pleuræ were infected in 7 of the 8 cases, and in most of them the infection was rather severe and extensive. Both hydrothorax and extensive obliterative pleuritis were encountered.

Lungs.—The lungs were absolutely free from *Paragonimus* infection in one of the 8 cases and in 1 it was confined to the lungs and pleuræ, and in still another the pleuræ was involved without invasion of the lungs. The lung lesions, consisting of pneumonic areas, abscess formation, infiltration of tissue, and bronchiectatic cavities, have already been described.

Pericardium.—Pericarditis, with eggs of the *Paragonimus* in the pericardium was present in 4 of the 8 cases.

Heart.—Brown, coarse and friable muscle was present 3 times and *Paragonimus* involvement extending a short distance beneath the epicardium was encountered in the same cases.

Abdominal cavity.—The tissues and organs of the abdominal cavity usually suffer severely in this disease.

The *omentum* was involved in 6 of the 8 cases and in most of these the distribution of the lesions was extensive.

Chronic peritonitis, consisting of adhesions between adherent adjacent organs, was usually a marked feature. The serous capsules covering the various organs also seemed to suffer extensively.

Diaphragm.—This organ was more or less involved in every case and in some it was fairly studded with lesions. In one instance only the pleural surface on the left side was involved and in another only the abdominal surface showed lesions.

Spleen.—*Paragonimus* lesions were scattered throughout the organ in one case; the capsule was similarly involved in two more and in one there was tuberculosis of the organ.

Liver.—There were changes for which the *Paragonimus* infection was at least partially responsible in 6 of the 8 cases. The most general disturbance was perihepatitis, with abscesses just beneath the capsule. In one, there were multiple abscesses containing both amœbæ and ova of *P. westermanii*. There were abscesses containing eggs in Glisson's capsule in one other case and in 2 more there was some cirrhosis with eggs in the hyperplastic connective tissue.

Pancreas.—In 2 cases there were *Paragonimus* abscess lesions in the pancreas.

Appendix.—There were parasitic lesions of the appendix in 4 cases. The meso-appendix suffered most, but in 3 the entire organ was affected and in 2 there was ulceration of the mucosa.

Stomach.—This organ was not involved in any instance with the exception of a few ahesions on the serous surfaces in 2 cases.

Small intestine.—There was infection of this organ in 6 of the 8 cases. In 3 the infection was severe and extended the full length of the gut. In 1 only the duodenum was concerned and in 3 others only the lower portion was affected.

Large intestine.—This organ was affected in 5 of the 8 cases. Tuberculosis was present in one instance. Amœbic and *Paragonimus* ulceration existed together in case 1 and there were amœbic lesions alone in another.

Kidneys.—The kidneys were included in the infection three times; the lesions were mostly closely connected with the capsule, but in 2 there were abscesses of the pelvis and in 1 the ureters were included in the affection.

Urinary bladder.—This organ had *Paragonimus* abscesses in the walls in 2 cases.

Scrotum.—The epididymis contained parasitic lesions in 3 instances; in 1 the infection extended through the inguinal canal to the abdominal lymphatics.

Prostate gland.—The prostate was involved four times. The lesions were of the abscess type and contained ova.

Brain and spinal cord.—These organs were only examined twice. In one instance there were *Paragonimus* lesions of the membranes of the brain, and eggs were found in the choroid plexus.

E. HISTOLOGY.

The literature bearing upon the microscopic study of the disease principally consists in the description of two types of lesion—the tubercle and the bluish-colored necrotic abscess.

The older literature is well summarized by Stiles and Hassall; since that summary was compiled, some original observations have been made, particularly by Katsurada. Looss has recently given another brief summary in Mense's handbook.

I shall discuss the lesions under the same classification as that already used in describing the gross pathology. They have certain points in common. In all the strictly parasitic types of infection there is the evidence of a slowly developing, low grade of chronic inflammation, with constant effort at repair which is chiefly manifested in the extensive proliferation of the connective-tissue framework, the new tissue being deposited about the original lesion, gradually encapsulating it or in some other manner tending to prevent its further spread.

This is made most manifest in the fully developed cystic abscess lesion, where the limiting wall is often very firm and thick. In other types it is less evident and in some of the very early infiltrations of the loose connective tissue with eggs it is entirely absent.

Eggs or parasites are by no means constantly present in any variety of the lesions. In the earlier forms the diagnosis can only be made by discovering the presence of these bodies, for there is nothing else characteristic about the lesions. The older ones and particularly those of the abscess variety take on characteristics which should be diagnostic even in the absence of eggs or parasites. Again, the greatest variation often exists in the number of eggs or parasites in a given lesion, sometimes the eggs are very numerous, and on the other hand, in an otherwise exactly similar lesion they may be very scarce. Parasites when present may range from one to many. More than 100 adult parasites were found in a psoas abscess.

The *nonsuppurative* lesions are of several types; however, some of these are but later stages of others, but there are certain ones which differ in formation as well as in their entire course.

The loose connective tissues, particularly in the subserous coat of the bowel, and less frequently elsewhere, may sometimes be found infiltrated with eggs without any decided change in the histology of the tissues themselves (Pl. X, fig. 1); however, in a later phase of this condition two changes begin to take place—a proliferation of connective tissue and beginning round cell infiltration. As the connective tissue wall developes in quantity, eggs may be surrounded by it, the proliferated cells increase in numbers and eventually the next stage is recognized—cirrhosis—or the lesion begins to break down and an abscess is formed. The early changes above referred to are rarely seen in the liver, but the second stage, with moderate cirrhosis by increase, particularly in the larger bands of Glisson's capsule, was present in one of my cases. After an examination of many specimens I have found a few eggs in apparently nonproliferating tissue of the liver.

The histology of broncho-pneumonia, another nonsuppurative type of lesion, does not differ materially from similar lesions due to other etiology. The exact method of formation is difficult to explain, but inasmuch as the two first stages of infiltration mentioned above are also seen in the lung, and bearing in mind the part played by the lymphatics in the distribution of the eggs, it would seem that the pneumonic areas, at least in part, may follow some of the other lesions.

Pneumonic areas sometimes become converted into the abscess type. The amount of embolism and thrombosis in this disease is exceedingly small. Lesions of the serous surfaces may be of the ordinary type, but often they have certain distinctions. They are most numerous about old adhesions, which may or may not be of *Paragonimus* origin. The adherent surfaces when separated are rough, raised, often of a brownish color, and contain eggs; sometimes these lesions break down and abscesses are formed. The histologic picture in these types shows a fibrosis, with very moderate round cell infiltration. Here, as in the other types discussed above, there is sometimes, but not often, a marked eosinophilia present.

Tubercle-like lesions, particularly those very much like miliary tubercles, have been mentioned by several writers. Miura states that they correspond histologically with Virchow's "fibrous tubercles," the centers containing eggs and often giant cells. These lesions have been considered the primary ones and all others the result of coalescence and changes in the tubercles.

Although lesions closely resembling more advanced tuberculosis are often encountered in these cases, I have not seen the type of miliary tubercle except in one case, and here the lesions were of true tuberculous origin. To judge from the descriptions of some of the cases in literature, it would seem that mixed infections such as were present in this case had been described. As has already been stated, eggs and tubercle bacilli have been found together in more advanced types of lesions and, as is

true in some other parasitic diseases, the infection seems to become more active in an already established lesion, let us say of tuberculous origin.

The abscesses are the characteristic lesions and they have been described in almost every article dealing with the disease. In brief they consist of three zones, the central one made up of necrotic tissue, degenerated cells and often of eggs or fragments of eggs; the middle coat consists of a more or less thick and dense fibrous capsule, formed of proliferated connective tissue, infiltrated to a moderate degree with round cells and sometimes with eggs. Its inner wall may be smooth and lined with epithelial cells, but it is often granular. The outer zone is one of moderate congestion, with proliferation of blood vessels and it is continuous with the surrounding tissues.

However, there is another type of abscess encountered most often in organs such as the prostate, epididymis, and the lymphatic glands, which histologically as well as in gross appearance more closely resembles an ordinary pyogenic abscess, and were it not for the presence of eggs or parasites such would surely be the diagnosis in many of these cases.

Ulcerative lesions are formed by the breaking through the mucosa or skin of any of the types already discussed, as a result of pressure, necrosis, thrombosis, or otherwise. This most often happens when the underlying lesion is an abscess, but it may take place with other types. In the intestine, the striking fact about these lesions is the usual absence of eggs or parasites in the mucosa, whereas the submucosa and deeper structures often contain them in large numbers and discharge them through the opening into the lumen of the bowel. This relative immunity of the mucous membranes to *Paragonimus* infection has already been mentioned, and it is in striking contrast to that with *Schistosoma* for example, where the mucosa is often infiltrated with eggs.

In the lungs this ulcerative process is probably the mode of formation of the bronchiectatic cavities. This is more probable than the belief that they result from a direct attack on the mucosa, or that they follow occlusion of a bronchus. In either case, the bronchial wall can and sometimes does take part in the formation of the abscess wall, but this, as has been emphasized by some writers, is not the rule. A moderate peribronchitis of quite general distribution in the smaller tubes is quite common in extensive lung involvement, but is more the result of the chronic bronchitis than of a *direct* influence by *P. westermanii*.

In the intestine, just as in the lung, the deeper structures and coats seem to be primarily involved, and the infection spreads through the subperitoneal muscular and submucous coats, often finding an outlet by ulceration of the mucosa. Frequently, however, ulceration does not take place even when tumors of the mucosa are pushed into the lumen of the bowel. Sections of one of this variety of lesion show a thickening of the connective-tissue layers, with proliferation of the fixed cells and

sometimes a marked eosinophilia. Mixed infection in any type of lesion may alter its histology very much, this alteration depending upon the nature of the secondary invader.

VIII. SYMPTOMATOLOGY.

A. GENERAL DESCRIPTION.

The clinical observations upon this disease have been largely confined to the symptoms of the pulmonary and cerebral types of the infection, and for these a summary of the literature gives a satisfactory picture of the disease as I have seen it. However, a study of the material upon which this report is based shows the disease to be much more generally distributed in the body than formerly it has been recognized to be, and therefore it necessitates a more comprehensive clinical picture than any which has previously been given. However, before taking up a consideration of these special types more in detail, it is necessary to discuss the general type of the disease in regard to its *acuteness*. Heretofore, it has been considered as being almost wholly a *chronic* infection, but some of my cases have shown a most acute and rapid course.

Acute and chronic processes.—It is probably a fact that the true and uncomplicated *Paragonimus* disease is always a chronic one, and that the more acute processes are the result of some concomitant infection or complication. This has already been pointed out as probably accounting for the rapid course of some of my cases and it is a condition which needs more study based upon a larger material. However, it is a fact that we must consider from a clinical standpoint at least some of these cases as acute, and while this condition obviously would be more likely to occur in a general infection, it surely may take place and influence the course and termination in some of the more restricted types.

B. CLINICAL TYPES.

After a careful study of the literature and of my own material, as well as I have had opportunity to do so, it seems advisable to consider the symptomatology under the following *arbitrary clinical* classification:

(*a*) Generalized paragonimiasis.
(*b*) Thoracic paragonimiasis.
(*c*) Abdominal paragonimiasis.
(*d*) Cerebral paragonimiasis.

(*a*) Generalized paragonimiasis.—A full consideration of the general infection would produce a composite picture of the other more local varieties, which I have already given in the classification and therefore, in order to avoid repetition, only those points in the clinical symptoms which are not directly covered in the discussion of the other clinical types will be noticed here. Some of the most interesting of these symptoms are produced by involvement of the superficial lymphatics and the skin. Enlarged lymph glands are quite common among the people of

this country, and cases of so-called "glandular fever" and of "climatic bubo" are not uncommon; some of these, as well as certain of the so-called "tropical ulcers," may have their etiology in trematode infections. The symptoms produced by glands infected with trematodes are not different from those of similar lesions of other etiology, and an exploratory incision may or may not reveal the presence of eggs.

The skin ulcerations have nothing characteristic. They are probably secondary to the infected lymphatics beneath. I found eggs in the contents of the ulcers in two of my cases, and the older and more advanced ulcers have a slate-colored, overhanging margin. The lack of evidence of acute inflammation about such ulcers is important.

One of my fatal cases, while in the hospital, complained of muscular rheumatic pains, and similar symptoms have been pointed out by other writers; this is at least partially explained by the distribution of the lesions, parasites and eggs in the muscular tissue.

Fever, which has not previously been considered an important symptom in these cases, was high in 4 out of 9 of mine and it probably will be found to be a somewhat constant symptom in extensive infections and in mixed ones which run a rapid course.

(*b*) Thoracic or pulmonary paragonimiasis.—According to the literature this is by far the most frequent type of the disease and locations of the infection other than in the thoracic cavity are considered to be secondary to this primary focus.

In two of my fatal cases and in two more of the clinical ones, the lungs were not involved and in several others the older and more severe lesions were surely present in the other organs. The pleuræ, diaphragm and other chest structures are so commonly, indeed almost constantly, involved with the lungs that thoracic paragonimiasis seems to be the more satisfactory term for this class of infection.

The most prominent symptoms ascribed to this type comprise: Pains in the chest; cough with occasional small hæmorrhages, the sputum containing eggs and according to Taylor and others sometimes an adult parasite. The physical signs are usually considered as being slight. Cough is a prominent symptom in most of these cases, but in one of mine it was so slight as to attract but little notice. The nature of the cough is as variable as that observed in tuberculosis, and the character and appearance of the sputum has an equally wide divergence; both depending largely upon the stage or nature of the underlying pathological change and the amount of lung tissue involved, together with the condition of the pleuræ and heart membranes, this condition depending upon the presence or absence of fluid, adhesions, etc. I have also convinced myself that the finding of eggs in the sputum in the average case requires more time and care than is usually supposed to be the case. Indeed, in one instance eggs were not found after several careful examinations made for this specific purpose, and yet at autopsy the lungs

and pleuræ were found to be involved. The number of eggs in the sputum depends upon the extent and particularly upon the *character* of the lesions. Just as is the case in tuberculosis, it is obvious that more of the eggs will be discharged from bronchiectatic cavities than from the equally important pneumonic areas. With this in view it seems hardly likely that *early* diagnoses are probable in this disease, and the need of *repeated* and careful search for eggs in the sputum of suspected cases is also emphasized. Hæmoptysis has not been a constant symptom in my cases, at least while they were under observation, but in one instance it was repeated and quite severe. In a country where tuberculosis is so very general, hæmoptysis would call attention to the disease under discussion only in the absence of other tubercular symptoms. Charcot-Leyden crystals are at times quite numerous in the sputum or again may not be observed at all. Other types of crystals, such as those of creatinin are also sometimes present. When the pleuræ are extensively involved, with but slight or no extension of the disease into the lungs, the chances of finding eggs in the sputum will be very small and the diagnosis will then have to be made largely from physical signs. The fluid from a *Paragonimus* empyema contains very few eggs and therefore, when this is the case, aspiration of the pleural cavities would often fail in furnishing a diagnosis.

In two cases under my observation which had pericarditis, the manifestations were similar to those encountered where this disease is of other etiology.

The physical signs in thoracic paragonimiasis have a greater importance than is usually ascribed to them. Bronchopneumonia, empyema, hydrothorax, etc., due to this infection show the same accurate physical signs as they do in the similar conditions produced by other causes. In one clinical case the presence of an empyema with pericarditis led to a careful examination of the sputum, and this determined the diagnosis. It must not be forgotten that, particularly in Manila, tuberculosis will be found associated with *Paragonimus*.

(*c*) Abdominal paragonimiasis.—This term is used by me to include the infection of any or all of the abdominal organs.

The abdominal infection is usually a rather extensive one and will hardly admit of a positive diagnosis without an exploratory operation or the finding of the eggs in the fæces. Eggs are probably only found in the fæces in the presence of ulcerative lesions in the bowel. In the several cases which I have had the opportunity of studying there was abdominal pain, mostly of a dull, aching character; in such instances the abdominal walls may be rather hard and may show some tenderness on pressure. In areas where the infection is endemic, hypertrophy of the prostate, cirrhosis of the liver, chronic epididymitis or lymphadenitis of doubtful etiology, should always lead to a careful study in which fluke infections are taken into consideration. If there is ulceration of

the intestinal mucosa, the eggs may be found in the fæces and there may or may not be diarrhœa. This fluke may possible at times be the etiologic factor in chronic appendicitis, but the infection will hardly be found confined to this organ.

(*d*) CEREBRAL PARAGONIMIASIS.—This important type of paragonimus infection was first recognized by Otoni and Inouye and since that time has received considerable discussion, particularly in its relation to Jacksonian epilepsy, of which it is one of the causes. Other prominent nervous symptoms consist in various forms of neuritis and even paralyses have been observed in this infection. Unfortunately, the brain and cord were removed in only two of my cases—in one because epilepsy was a prominent symptom during the short time the patient was under observation.

C. PARAGONIMIASIS OF THE LOWER ANIMALS.

P. westermanii is known to infect the tiger, cat, dog and hog, but as has been pointed out by Stiles and Hassall, very little is known of the symptomatology and pathology of the disease in these animals. Since the discovery about one year ago of the first case of this infection in man in the Philippine Islands, the following animals have been carefully examined for fluke infection:

Thirty-two cats with 1 positive result for *P. westermanii* and in 17 others *O. felineus* was encountered; 23 dogs with no case of infection with *P. westermanii;* 10 rats and mice with no case of fluke infection of any kind.

Paragonimiasis of the cat.—The case of one animal in which this infection was encountered in the Philippines is interesting. The animal was purchased from a native and was placed in a large cage with several others and left for about one week. When received it was rather thin, but otherwise apparently healthy. At the end of a week it was brought to me by the animal care-taker in a dying condition. Emaciation was marked, food was refused, there was diarrhœa and partial paralysis of the hind quarters. The animal was chloroformed and autopsy performed at once. *Paragonimus* lesions with eggs and parasites were found in the lungs, intestines and omentum. The lesions were not extensive and both these and the parasites were apparently identical with those found in man.

IX. DIAGNOSIS.

A direct, positive diagnosis of paragonimiasis can only be made by the finding of parasites or eggs. Under favorable conditions the eggs may be encountered in the sputum, fæces, scraping from ulcers, and in fluids and tissues removed by operation.

The sputum should be examined as a cover-glass preparation of a fresh specimen and, in suspected cases, the examinations should be frequently and carefully made during considerable periods of time. The eggs are easily recognized under the lower powers of the microscope;

their outlines may be made sharper and clearer and the operculum may be rendered more distinct by adding a small quantity of dilute sulphuric acid to the specimen, or by running a drop or two of a 0.1 per cent solution under the cover glass. The ordinary munipulations used in preparing a specimen of sputum for examination for tubercle bacilli either destroy the eggs or reduce them to an unrecognizable condition. Once, in examining a slide for tubercle bacilli, peculiar appearing bodies were noticed, which led to the examination of a fresh specimen and to the recognition of a case of paragonimiasis which had previously been unsuspected. This patient also had tubercle bacilli in his sputum. While in several conditions Charcot-Leyden crystals are found in the sputum, they are in this disease more numerous and constant than the eggs of the parasite, and when seen in considerable numbers in a sputum from a patient in regions where the infection is endemic, their presence should lead to a closer investigation for *Paragonimus* disease. In the Philippine Islands, and other endemic zones, examinations of fresh specimens of sputum should be as much a part of routine as is the examination of stained ones.

Fæces.—Several times duirng the past year the presence of *Paragonimus* infection has been discovered by finding the eggs in the fæces. In one case the diagnosis was confirmed by an autopsy. In two of these instances no eggs could be discovered in the sputum. Only a simple cover-glass preparation is needed for the examination of the fæces and the eggs are most quickly located with an AA objective and a number 4 occular. The eggs are less numerous in the fæces than they are in the sputum, and they usually are found only after persistent search.

The primary lesions in the intestine are usually in the deeper layers and the eggs probably do not appear in the fæces unless there are ulcerations of the mucosa; this fact has been pointed out in the discussion of the pathology of this disease.

Ulcers.—Ulceration of the skin of a chronic type leading into deeper tissues should indicate careful examination of the scrapings for eggs of *P. westermanii.*

Fluids and tissues removed by surgical operation in obscure cases should be carefully scrutinized for eggs and parasites in zones where the disease is endemic. This is particularly true in operations which require the opening of the abdominal or pleural cavities.

In exploratory, diagnostic operations in the Philippine Islands, particularly upon the chest, abdomen, liver, scrotum or prostate, fluke infections should be kept in mind. The difficulty of distinguishing the egg of *P. westermanii* from some of the other fluke eggs has already been noticed in another part of this paper and need not be repeated here.

While, as stated above, positive diagnosis can only rarely be made in the living subject except by finding parasites or eggs, there are several subjec-

tive symptoms and physical signs which furnish strong supporting data. Of these the following, occurring singly or together, may be noticed: Unexplained epilepsy or other evidence of localized brain lesions; cough with occasional small amounts of blood, particularly with but slight or no constitutional disturbance and with broncho pneumonia and empyema. Evidences of chronic peritonitis, enlarged prostate, epididymitis, or cirrhosis of the liver, and chronic skin ulceration with enlargement of the lymphatic glands.

Owing to the slow progress of the disease in many cases and to the probable late appearance of ova in the excreta, many of these infections will continue first to be diagnosed at autopsy, until other accurate diagnostic data are available.

X. COURSE, DURATION AND PROGNOSIS.

The course is usually chronic, the disease lasting for years; however in some cases, and particularly in mixed infections, it may be acute, and death may result in a few days from the time the symptoms are first noticed. Several writers have stated that patients may live for fifteen or even twenty years.

The prognosis, if the patient remains in the region where the infection is endemic, is usually bad as to recovery, although several writers say that this may take place. After a study of the pathology of the disease, this statement seems difficult to believe. Evidence is sometimes found indicating that there may be an arrest of the progress of the disease, and were this to occur in the early stages of the infection, the patient might remain in good condition for many years. However, with the usual types of the disease it is doubtful if complete healing of the pathologic process ever takes place.

Death probably most often is caused by intercurrent diseases, but in at least two of my fatal cases no evidence of such a condition was found at autopsy.

XI. COMPLICATIONS.

While it is probable that a great variety of diseases may be found associated with paragonimiasis and while other diseases often develop during the course of this infection and hasten its outcome, there are but two which, because of their special importance, will be noticed here. These are tuberculosis and amœbiasis.

Tuberculosis, either local or general, may complicate either a local or more general distribution of the parasitic disease. The two diseases existed together in 2 of my 8 fatal cases and such a combination has in addition been found 3 times clinically. There are several reasons why this particular complication should receive close attention. The symptomatology of the two diseases is often very similar. The lesions are

sometimes rather difficult to distinguish, and the two infections may be found co-existent in the same lesion.

Amœbiasis complicated 3 of my fatal cases, and the two diseases have been found together twice clinically. The association is particularly interesting in case 1, where both etiologic agents were found together in the multiple abscesses of the liver and in lesions in several other parts of the body.

It is probable that in intestinal paragonimiasis eggs would more readily be found in a bowel already ulcerated by amœbæ. The symptomatology of the two diseases, when the abdominal organs are particularly involved by the *Paragonimus,* may be very similar and the double infection easily overlooked.

XII. PROPHYLAXIS.

As has been pointed out by Stiles and Hassall, Looss and many other writers, no satisfactory prophylaxis against this disease can be established until the life cycle of the parasite has been elucidated. General hygienic usages are recommended by most authors, these measures, for example, being the use of cooked food and sterilized water and the disinfection of the sputa of infected hosts. In addition to the lack of knowledge of the complete life cycle of the parasite, successful prophylaxis is further inhibited by an ignorance of the complete list of the hosts of the adult fluke in zones where the parasite is endemic and its prevalence in these different species of animals.

Practically all writers have assumed that the infection takes place through the gastro-intestinal canal, and this is probably true, but it seems that the question of possible infection through the skin should also receive careful consideration. The frequent, extensive involvement of the lymphatics and the rôle played by this system in the distribution of the infection in the body of the animal host make it very important that skin infection be excluded in considering the manner of entrance of the parasite. The probable similarity between the life cycle of this fluke and that of some others with known life histories, adds another good reason for forbidding the use of uncooked food, particularly vegetables and water, in countries where the disease is endemic. For similar reasons it seems justifiable particularly to warn against the consumption of uncooked fish, clams, crabs, oysters and other shellfish obtained from local waters. From data brought out in this report it seems wise to recommend not only the destruction of the sputum of infected human hosts, but an equally careful disposition of the fæces and, in cases where ulceration of the skin exists, careful disinfection or destruction of the dressings should be a routine procedure. Finally, it seems that the spread of the disease might be somewhat limited by the destruction of as many of the lower animal hosts as can be discovered. In this country

cats, dogs and pigs are very numerous; they enjoy unusually close relations with members of the community, and in the absence of a satisfactory means of the disposal of their excreta these must always prove a menace in infecting the probable harborers of the other phases of the life cycle of the parasite.

XIII. TREATMENT.

No form of treatment so far established is specific against the infection. Many different types of therapeutics have been used and some of them, such as inhalations of antiseptic substances for the pulmonary type, have been thought to benefit the patient.

Taylor recommends rest in bed during times where there is hæmoptysis or when the cough is very severe.

A general, tonic treatment, consisting both of good hygienic measures and drugs, is recommended by all observers and a change of climate to noninfected regions urged by some.

In one of my cases the cough disappeared and the general condition of the patient improved very much under large doses of potassium iodide.

XIV. LITERATURE REFERENCES.

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ILLUSTRATIONS.

PLATE I. Heart showing adult parasite (at *a*) and the raised brownish colored areas infiltrated with eggs described in the text.

II. Fig. 1. Lung showing pneumonic areas, one early abscess lesion, section of adult parasite in a bronchus and another in a pneumonic area.

Fig. 2. Lymphatic gland, showing necrotic lesion from which adult parasite was removed.

III. Adult *P. westermanii*, showing subterminal oral sucker, acetabulum, genital pore, excretory pore and intestinal cæca.

IV. Fig. 1. Egg of *P. westermanii*, showing cellular contents; operculum not in good focus.

Fig. 2. Fresh smear from *Paragonimus* abscess of spleen, showing eggs.

V, figs. 1–9, and Plate VI, figs. 1–9, represent 18 selected specimens from serial sections of the adult parasite cut longitudinally. Sections of all the important structures may be seen in these figures.

VII, figs. 1–9, and Plate VIII, figs. 1–9, are similar to Plates V and VI, except that in the former the sections are cut transversely.

IX. Fig. 1. From the subserous coat of the intestine, showing numerous eggs; otherwise but slight change in the tissues. × 35.

Fig. 2. From intestinal wall, tissue containing eggs, with cellular infiltration. × 35.

X. Fig. 1. From the intestinal wall, showing connective-tissue hyperplasia, cellular infiltration and necrosis, with many eggs.

Fig. 2. Typical, small necrotic lesion removed from lymphatic gland. × 46.

XI. Figs. 1 and 2. Both figures show sections through large abscess lesions containing adult parasites.

PLATE III.

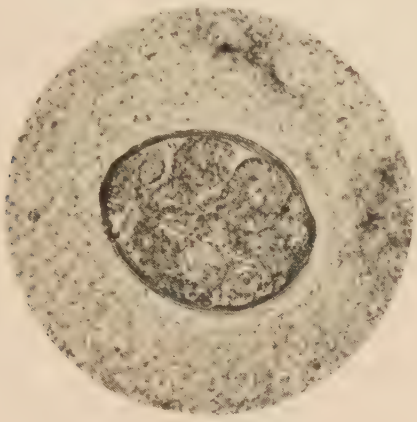


FIG. 1.

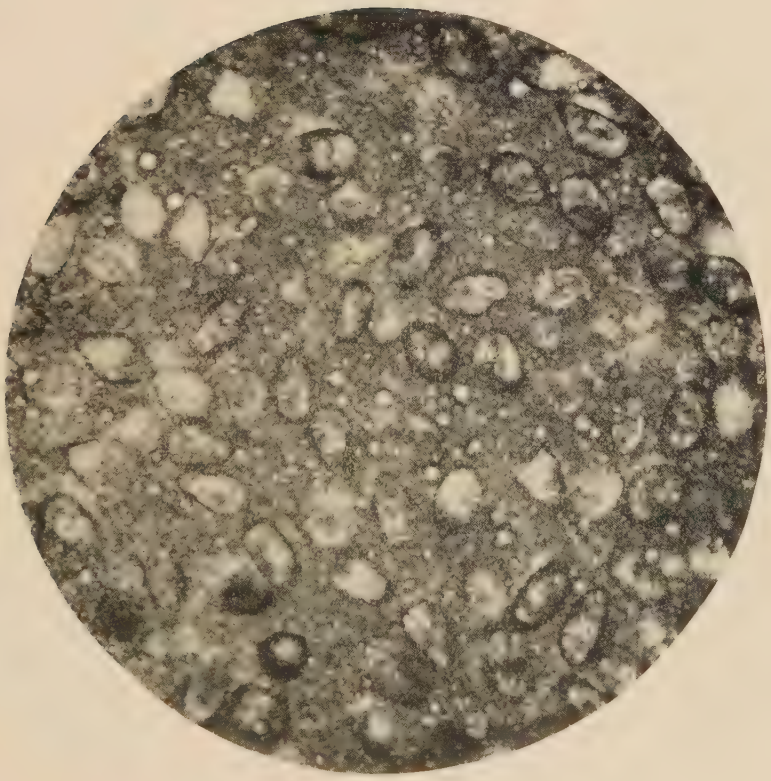


FIG. 2.

PLATE IV.

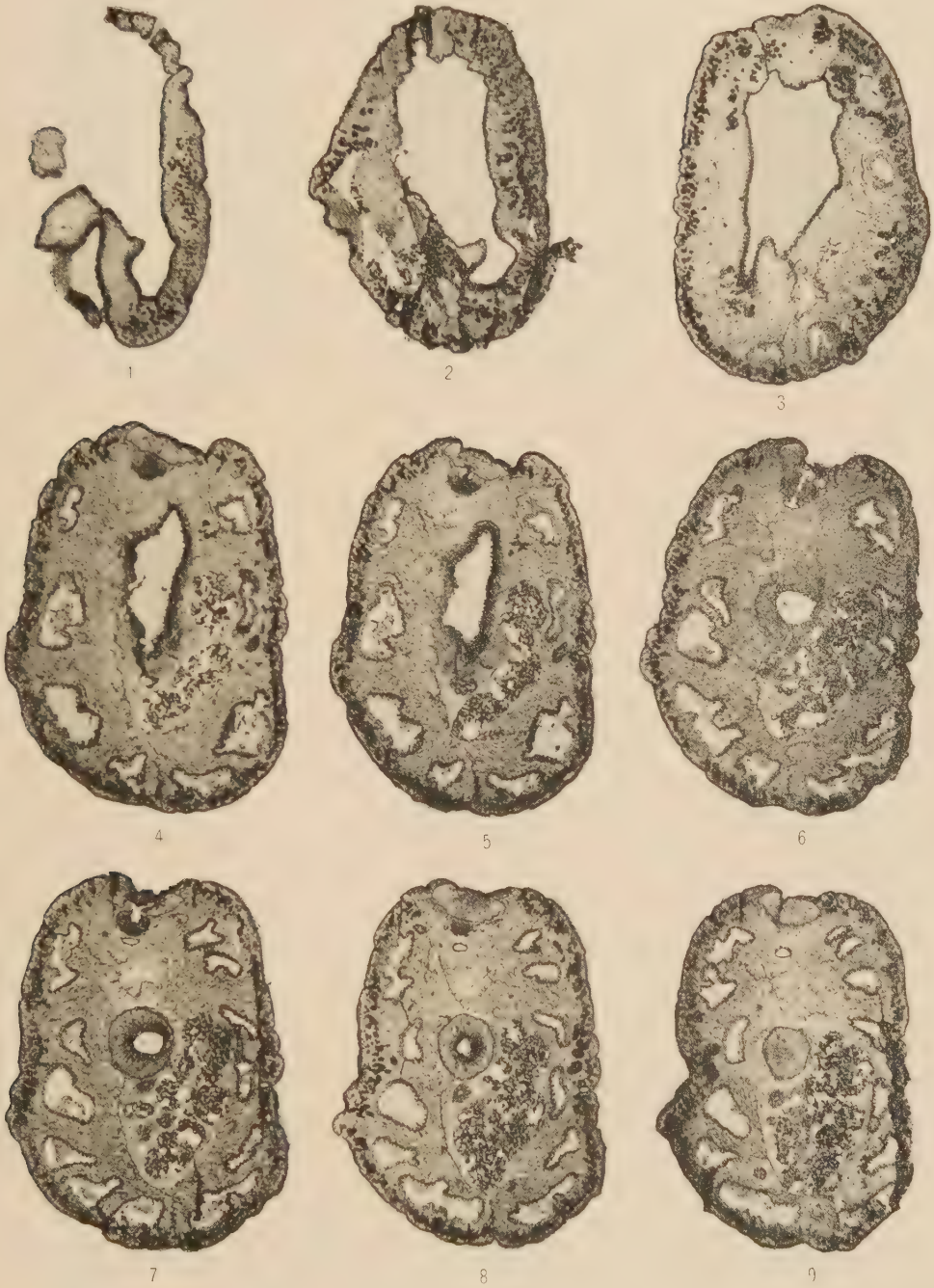
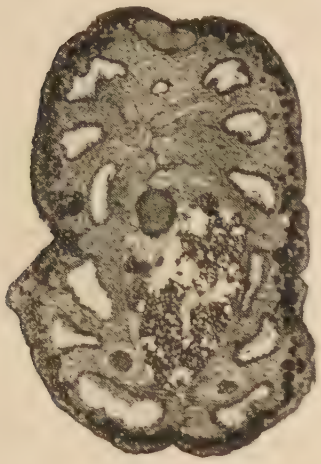


PLATE V.



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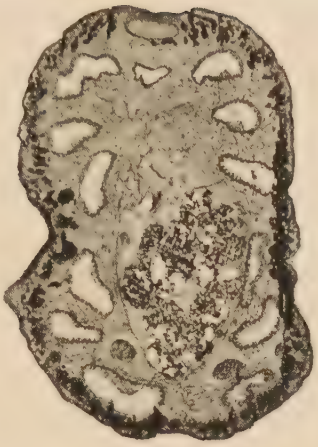

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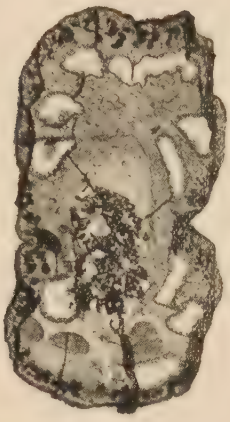

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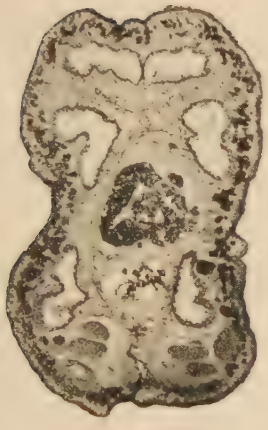

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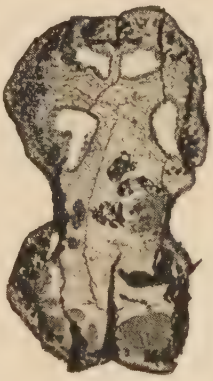

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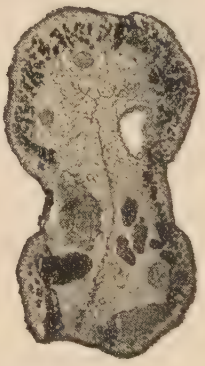

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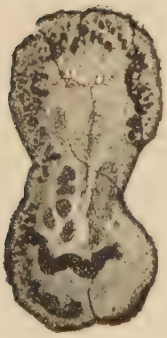

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PLATE VI.

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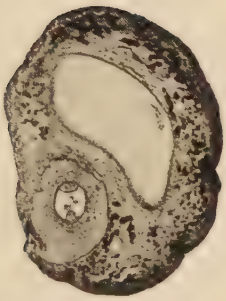

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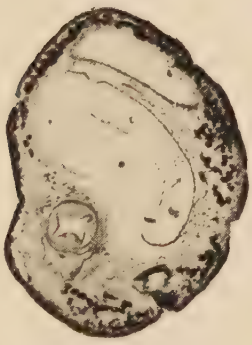

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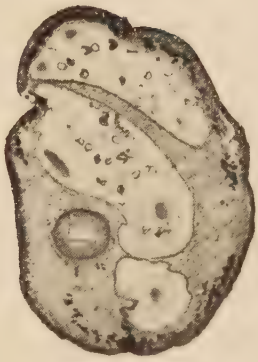

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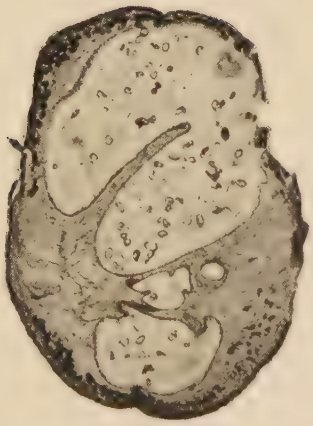

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PLATE VII.

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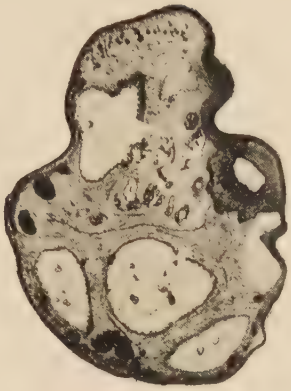

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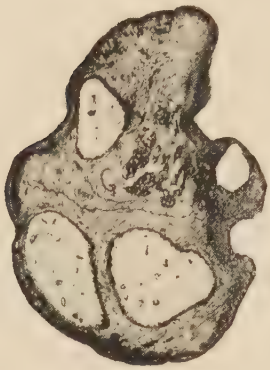

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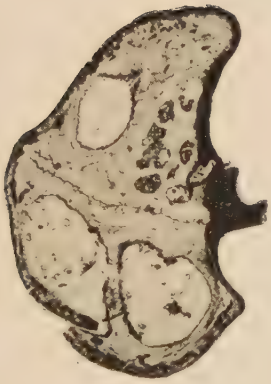

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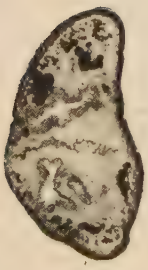

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PLATE VIII.

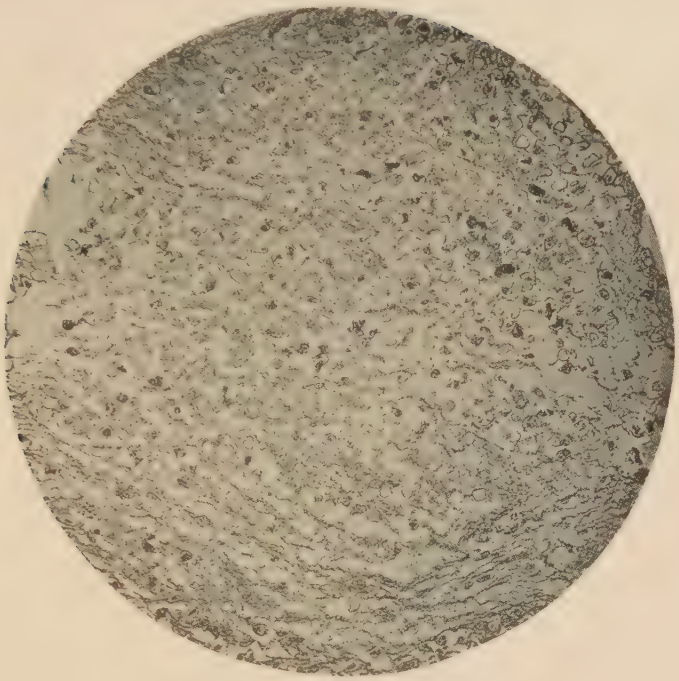

FIG. 1.

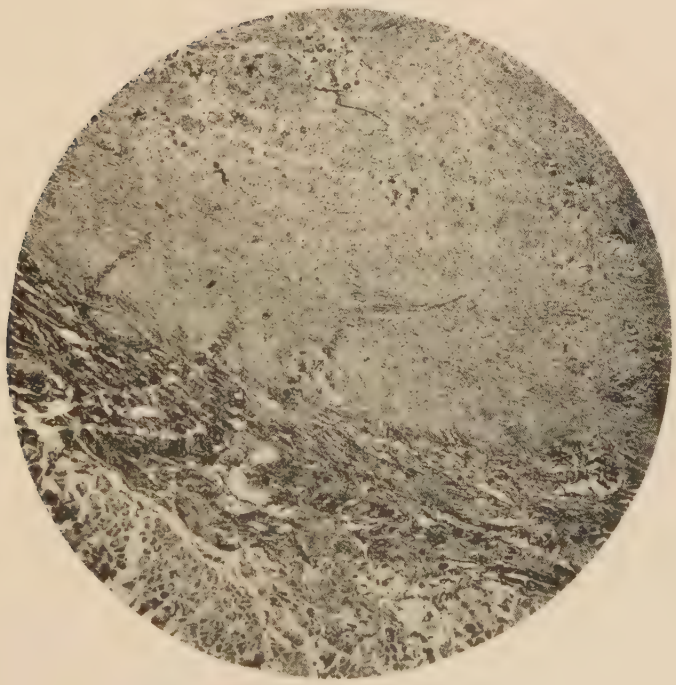

FIG. 2.

PLATE IX.

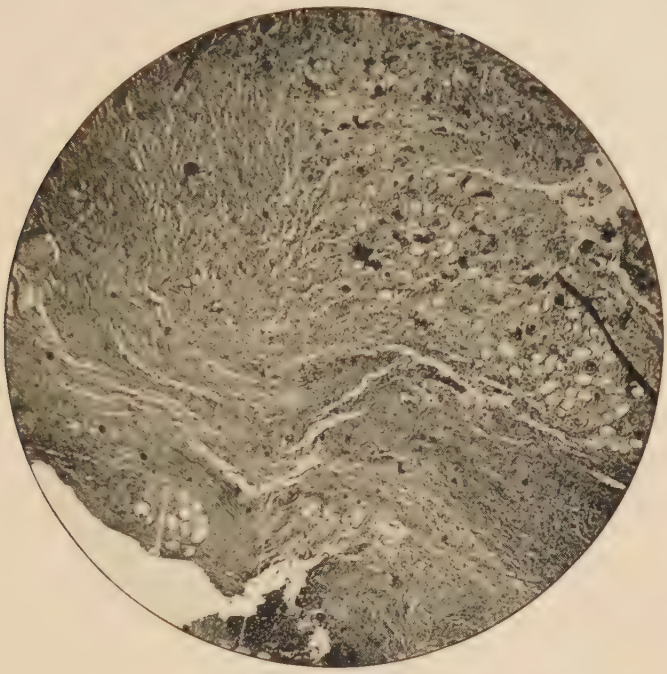

FIG. 1.

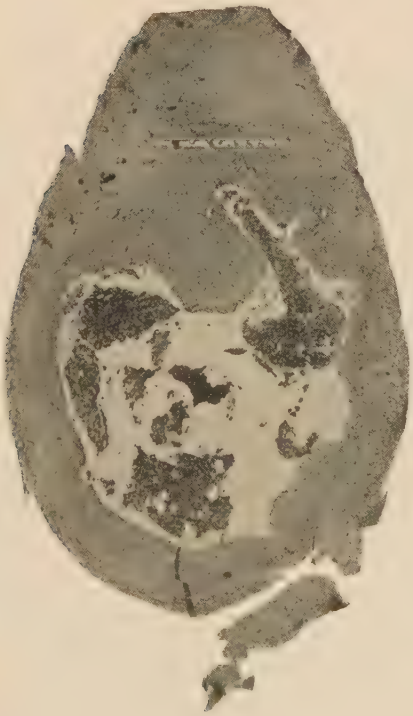

FIG. 2.

PLATE X.

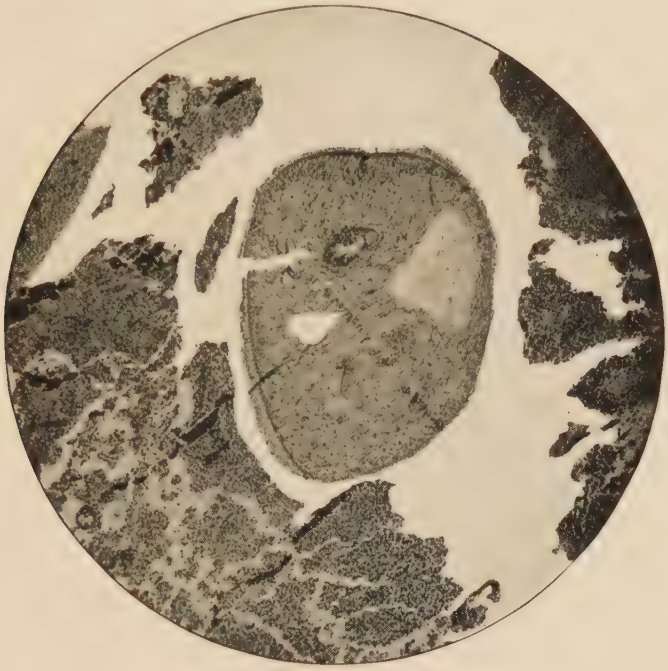

FIG. 1.

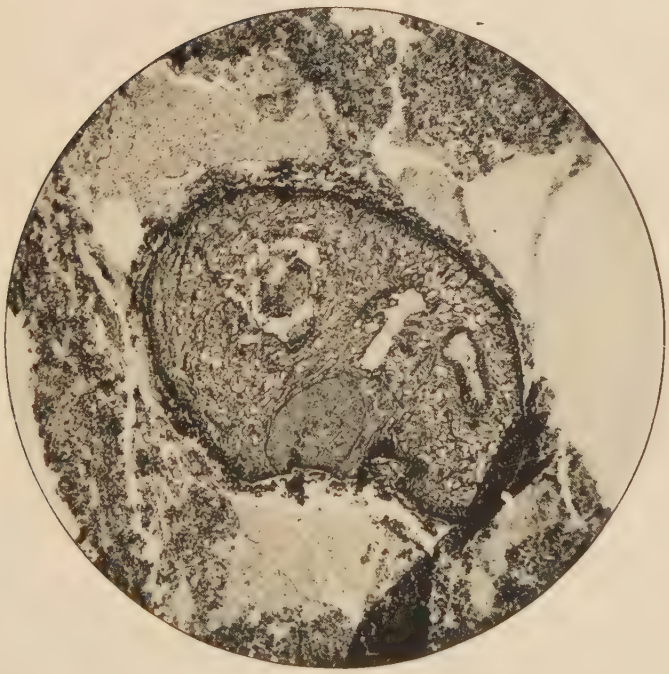

FIG. 2.

PLATE XI.

REVIEWS.

A Compend of Genito-Urinary Diseases and Syphilis, Including Their Surgery and Treatment. By Charles S. Hirsch, M. D. Cloth; 70 illustrations in the text; 1 plate. Pp., xvi + 351. Price, $1.00. Philadelphia: P. Blakiston's Son & Co., 1906.

The abortive treatment of gonorrhœa is given a place in this book, though it does not enter into the modern treatment of the disease.

The metric systm is not used, nor are the metric equivalents of the apothecaries' weights and measures, which latter are used throughout, given. It is much to be desired that all American text-books on scientific subjects either be printed in the metric system or give metric equivalents for other terms used.

In the treatment of the seminal duct and vesicle no mention of the very valuable treatment of chronic affections of these organs by irrigation and drainage of the seminal ducts and vesicles through the vas deferens is made, although Belfield's first paper on this subject was published in the Journal of the American Medical Association in April, 1905.

In the article on circumcision silk sutures are recommended. Silk, as either a suture or ligature material, has scarcely any place in modern surgery and especially not in operations upon parts of the body much exposed to contamination by the excretions.

Under the treatment of the infection of the bladder, vesical amœbiasis is not mentioned.

The statement that suprapubic cystotomy is contraindicated in children is contrary to the best modern surgical practice. The suprapubic method is preferred by surgeons to the perineal operation in children, especially young children, if the calculus is too small or too hard to be easily removed by crushing. The article on suprapubic cystotomy tells us that the bladder must be tightly sutured about the drainage tube for fear of infecting the prevesical space by the escaping urine. This is not necessary. There need be no fear of infection of the prevesical space so long as there is free drainage.

We are told that a floating kidney may be retained in position by a pad placed over the cæcum. Assuming that this treatment is intended

for the right kidney we are left in the dark as to where the pad is to be placed in case the left kidney be displaced.

The table of differential diagnosis between epithelioma and chancre states that the microscopical examination of the latter is negative, yet we are told in the foregoing that the *Spirochaeta pallida* is the most probable infecting agent causing the manifestations termed syphylis and that it may be demonstrated in the initial lesion of the disease.

The intramuscular injection of mercury as a means of treatment in syphilis is not given as much prominence as its increasing popularity among syphilographers would seems to warrant. Bichloride of mercury is given first place. It is well known that this is the most irritating of all salts of mercury when so used.

The book contains about 150 typographical errors. An example of some of the most glaring is the use of the term "nephrectomy" for "nephrotomy" under "Cysts of the kidney," page 193.

We never approved of medical compends. They must necessarily omit much that is essential and can not take the place of more thorough reading when they fall into the hands of students, as they usually do. When carelessly printed they are a real evil.

F. W. D.

A Compend of Materia Medica, Therapeutics and Prescription Writing, with Especial Reference to the Physiological Action of Drugs. Based on the eighth revision of the United States Phamacopœia. By Samuel O. L. Potter, M. D., M. R. C. P., Lond. Seventh edition, revised and enlarged. Cloth. Pp., xii + 292. Philadelphia: P. Blakiston's Son & Co., 1906.

The book fulfills the objects of a quiz-compend in that a large amount of information is presented in a systematised and greatly condensed form. Discussions are avoided, and the style is one of short, dogmatic assertion, which is possibly more suitable for a student cramming for examination and memorizing automatically. It is difficult to share the optimism evidenced by the author as to the therapeutic value of certain drugs, and greater discrimination in this regard would increase the accuracy of the book. Thus, the thyroid gland or its extract is described as specific against psoriasis, obesity and certain forms of insanity; antidiphtheric serum is noted to have benefited typhoid fever, pertussis and asthma.

The printing and binding conform to the rest of the series. The dosage is given according to apothecaries' measure, without metric equivalents.

H. T. M.

The American Illustrated Medical Dictionary. A new and complete dictionary of the terms used in medicine, surgery, dentistry, pharmacy, chemistry and the kindred branches, with their pronunciation, derivation, and definition, including much collateral information of an encyclopedic character. Fourth edition, revised and enlarged. Limp morocco. Pp., 836; 18 illustrations in the text and 29 plates, 28 of which are colored. Price, $4.50. Philadelphia and London: W. B. Saunders Company, 1906.

The present revised edition of this work is, like its predecessors, thoroughly up to date. It furnishes to the student in portable form just what he needs and saves the busy practitioner much valuable time. So far as we have been able to ascertain all the new terms have been included and the semi-encyclopædic character of the work combined with its compactness leaves little to be desired. The author's wide experience both as teacher and physician has enabled him to appreciate what is most needed, and with infinite labor he has condensed the information usually only available in an encyclopedia of medicine into 836 octavo pages. The tables and illustrations are such as are of practical value, and printing and binding are in accordance with the general excellence of the work.

E. C. S.

Stöhr's Histology Arranged upon an Embryological Basis. By Dr. Frederick T. Lewis. From the twelfth German edition by Dr. Philipp Stöhr. Sixth American edition. Cloth; 450 illustrations in the text, 45 of which are colored. Pp., ix + 434. Price, $3.00. Philadelphia: P. Blakiston's Son & Co., 1906.

Dr. Lewis has proved very successful in continuing Dr. Shaper's American edition of Stöhr's Histology.

The arrangement of the book is good. Following a brief but clear description of the structure and vital phenomena of the cell, 134 pages are devoted to general histology and 248 pages to the special systems. A chapter on technique and an excellent index complete the volume. The distinctive feature of the book is the arrangement upon an embryological basis. The description of the adult tissue, or organ, is preceded by a review of the embryogeny, thus enabling the student to gain a comprehensive grasp of the subject and to form a logical conception of the significance of the part studied. The value of the book has been further enhanced by the adoption of the newer anatomical nomenclature. The illustrations, of which there are 450, are in general satisfactory, many presenting early stages in development. It may be suggested that the study of the brain would be simplified by adding a few illustrations at different levels through the medulla, pons, and crura cerebri.

The printing is clear, the size of the volume convenient, and the book can be highly recommended to the student.

H. T. M.